DOES NOT CIRCULATE

UNIVERSITY OF MICHIGAN

FEB 7 1955

MEDICAL LIBRARY

BRITISH MEDICAL JOURNAL

JOURNAL OF THE BRITISH MEDICAL ASSOCIATION

SATURDAY JANUARY 15 1955

TABLE OF CONTENTS

The Circle of Willis Sir CHARLES SYMONDS, K.B.E., C.B., D.M., F.R.C.P. 119
Pancreatitis Following Pregnancy R. A. JOSKE, M.D., M.R.A.C.P. 124
Tuberculous Mesenteric Adenitis in Children HUGH R. E. WALLIS, M.D., M.R.C.P., D.C.H. 128
A Comparison of Vaccination with Vole Bacillus and B.C.G. Vaccines HUGH W. O. FREW, M.D., D.P.H., J. ROMANES DAVIDSON, M.D., and J. T. W. REID, M.B., D.P.H. 133
Treatment of Papilloma of Bladder with Radioactive Colloidal Gold Au^{198} FRANK ELLIS, M.D., M.SC., F.F.R., and R. OLIVER, M.SC., A.Inst.P., A.M.I.E.E. 136
Spinal Disk Lesions JAMES CYRIAX, M.D., M.R.C.P. 140
Primary Tumours of the Small Bowel T. A. OGILVIE, M.B., F.R.C.S.Ed., and H. M. SHAW, M.B., F.R.C.S. 142
Association of Jejunal Diverticulosis and Steatorrhoea A. P. DICK, M.D., F.R.C.P. 145
Antibiotic Sensitivity Spectra E. P. SILBERSTEIN, M.B., B.SC. 148

MEDICAL MEMORANDA

Two Cases of Favism in Israel. S. MANSOOR, M.D. 149
Rheumatoid Arthritis treated with Organic Copper Compounds. T. J. O'REILLY, M.D. 150
Fat Embolism in Thoracic Operations. FLORENCE MCKEOWN, M.D. 150

BOOK REVIEWS 151

REFRESHER COURSE

Shock. Sir HENEAGE OGILVIE, K.B.E., M.D., M.Ch., F.R.C.S. 159

GENERAL ARTICLES AND NEWS

BACTERIAL GENETICS 161
SOCIAL PROBLEMS OF THE YOUNG DISABLED 163
VITAL STATISTICS 173
MEDICAL NEWS 175
BIRTHS, MARRIAGES, AND DEATHS 176

OBITUARY

Sir Arthur Keith, M.D., LL.D., D.SC., F.R.C.S., F.R.S. 168
Claude Rundle, O.B.E., M.D., D.P.H. 171
H. N. Webber, B.chir., F.F.A. R.C.S. 172
G. W. Miller, D.S.O., M.B. 172
Charlotte R. Brown, M.D. 173

LEADING ARTICLES

Family Census 153
Rugby Football Injuries 154
Tuberculous Mesenteric Adenitis in Children 155
Sterilization Methods 156

ANNOTATIONS

Papillomatosis of the Bladder 157
Eyes and Appetite 158
Edinburgh Medical Journal 158

CORRESPONDENCE

Low Backache. JOHN CHARNLEY, F.R.C.S. 163
Anaemia of Newborn. G. A. NELIGAN, M.R.C.P., and J. K. RUSSELL, M.B. 164
Pure Red-cell Anaemia. H. S. BAAR, M.D. 164
Tuberculosis. J. F. BRAILSFORD, M.D. 164

SUPPLEMENT

Full Contents on First Page of Supplement
L.C.C. Health Report 15
Residential Accommodation for Hospital Staff 16
Medical Practices Committee 16
Correspondence:
Practice in the Highlands and Islands. J. GUTHRIE, M.B. 17
Local Health Authority Nursing Services. C. H. B. LAWFIELD, M.R.C.S.; N. A. JEVONS, L.M.S.S.A.; S. T. BEGGS, M.D. 18

CORRESPONDENCE—*cont.*

Premedication for Tonsillectomy. F. R. GUSTERSON, D.A. 165
Mobile Physiotherapy Unit. H. S. ATKINSON, B.M. 165
Intussusception in Newborn. T. DE VEGA RUIZ, M.D. 165
Rupture of Retro-pharyngo-oesophageal Abscess. K. E. PEMBREY, M.R.C.S. 165
Carcinogens in Cigarette Smoke. M. SEGAL, B.SC. 165
Paget's Disease. H. RHYS DAVIES, M.D. 166
Operator and Anaesthetist. R. BLAIR GOULD, M.B., F.F.A. R.C.S. 166
Chlorpromazine. D. A. B. HOPKIN, M.D., F.F.A. R.C.S. 166
Herpes Zoster. K. E. JOLLES, M.R.C.S. ..166
Footnote to History. W. A. RAMSAY, M.D. 167
Kaposi's Varicelliform Eruption. A. BIGHAM, M.D.; B. F. RUSSELL, M.D. ..167
Still Going Strong. K. I. E. MACLEOD, M.D. 167
Pre-operative Transhepatic Cholangiography. D. H. PATEY, F.R.C.S. 167

QUESTIONS AND COMMENTS

Treatment of Salmonella Carriers—Surgery in Congenital Pulmonary Stenosis—Toxic Effects of Amphetamine—Blushing—Prosthesis after Mastectomy—Two Cases of Fetishism—Treatment of Meningococcal Meningitis—Tincture of Belladonna 177-8

BRITISH MEDICAL ASSOCIATION, TAVISTOCK SQUARE, LONDON, W.C.1

No. 4906, WEEKLY, PRICE 3/-

Copyright

REGISTERED AS A NEWSPAPER

Setting The Right Course...

The RIGHT direction for Savings

The Compass is a symbol of progress. For thousands of years it has guided seamen in trust and confidence across the waters of the world. Progress, too, is the guiding principle of the Unit Trusts in the 'Bank-Insurance' Group which have grown and appreciated over the years. Today the course of our Units is confidently followed by investors, trusting in the cardinal points which have established this group's policy :—

STABILITY by investing in banks, insurance companies and investment trusts.

SECURITY by spreading the risk.

CONFIDENCE from the public who invest.

PROGRESS through careful management.

PRICE & YIELD OF ONE OF OUR TRUSTS

CONSOLIDATED UNITS

of Bank, Insurance and Investment Trust Securities.

11th January—Offer price 20/3*xd. Yield* £3 12s. 11d.%

TRUSTEES :

MIDLAND BANK EXECUTOR AND TRUSTEE COMPANY LTD.

Full particulars including prices and yields of all Units in the 'Bank-Insurance' Group together with an explanatory leaflet may be obtained from your stockbroker, banker, solicitor or accountant or direct from the Managers :—

BANK INSURANCE TRUST

CORPORATION LIMITED

30 Cornhill, London, E.C.3

Scottish Agents: Scottish Bank Insurance & Trust Shares Limited
5 St. Andrew Square, Edinburgh, 2

CVS-27

ASTHMA

SPECIAL NOTICE

The Ministry of Health have agreed our new prices of RYBARVIN *and* RYBAREX *and approve their prescription on form* E.C. 10.

RYBAR
LABORATORIES LTD.
TANKERTON · KENT

PB 14

When a gentle laxative is needed... Andrews Liver Salt may be indicated

Effervescent

Pleasant-tasting

APPROX. COMPOSITION	
Tartaric Acid	23%
Sodium Bicarbonate	23%
Magnesium Sulphate (B.P.C. Exsicc)	17%
Sugar	37%

We shall be pleased to send an 8 oz. tin for clinical trial, on request
SCOTT & TURNER LTD. ANDREWS HOUSE NEWCASTLE-UPON-TY

BRITISH MEDICAL JOURNAL

LONDON SATURDAY JANUARY 15 1955

THE CIRCLE OF WILLIS*

BY

Sir CHARLES SYMONDS, K.B.E., C.B., D.M., F.R.C.P.

Physician for Nervous Diseases, Guy's Hospital; Physician, National Hospital, Queen Square

My first task is to thank you, Mr. President, Fellows and Members of the College, for appointing me to make this Oration according to Harvey's instructions, wherein he designed the pattern for a tradition now almost three centuries old. Whoever is charged with the duty must feel at this moment proud of the honour and humbled by the greatness of the occasion.

Of the directions given to the Orator two are simple —to commemorate the benefactors of the College, and to bid you continue in mutual love and affection among yourselves. The other is the exhortation to the Fellows and Members to search and study out the secrets of Nature by way of experiment. In this connexion we must remember that Harvey was what to-day would be called a physiologist. It is true that he practised medicine, but not very much, nor, according to one of his biographers, very well (Anon., 1830). His great discoveries, including that of the circulation of the blood, were based mainly on observations upon animals. It was natural, therefore, that he should direct the Orator to appeal for recruits to this branch of learning, and that the appeal should be addressed to the Fellows and Members of the College, for it was only physicians who were then qualified for this work. Since then the scene has changed. There is specialization of function such as Harvey could not imagine. The physiologist and physician are different persons.

The Urge to Discover

Moreover, the science of medicine, which had hardly begun in Harvey's day, now has values of its own which he would doubtless have found satisfying. He would not, I am sure, have wished you all to turn physiologists. He would none the less have urged you to prosecute research. This, I believe, is what most of us want to do when we enter the practice of consulting medicine, and for many of us the urge to discover something new is one of the motives that directs our choice of career. We start with enthusiasm, but the later results are on the whole disappointing. For this there are many reasons, of which the first and most obvious is that to want to do a thing well is not the same thing as having an aptitude for it, but I do not think this is so widely applicable as is sometimes supposed. Another reason often given is that research in medicine is a full-time employment, with the implication that a man must choose between research and practice. This idea has been fostered by the growth of units whose senior members give the whole of their time to clinical research and are not engaged in the ordinary practice of medicine.

It is true that the whole-time clinical research worker has great advantages, from which he has not been slow to profit. Witness the volume and quality of the work published from these units during the past thirty years. The practising physician also has some advantages, which are not so apparent and deserve mention. One lies in what I may call the range and intensity of his exposure to stimulus. He goes to his out-patient clinic, his wards, or his consulting-room not knowing in the morning what the day will bring to him of the phenomena of disease. No sooner has he focused his attention on one problem than it is switched to another. At the end of the day his mind carries a load of unanswered questions. This you may say is distracting and an impediment to thought, but the variety of experience has a value.

There is much darkness in the world of medicine, and light may come from an unexpected quarter, so that the man who is compelled to shift his gaze from one point of the compass to another may be better off than he who is always looking in one direction. It may happen to those wholly engaged in clinical research that they miss the opportunity of seeing in matters outside their scope something of fundamental importance to their inquiries, while to the practitioner chance may offer a new concept of disease from the observation in the same week of two cases which are clearly alike but like nothing else that has ever been seen. For the practising physician also the unanswered questions are perhaps more often invested with a sense of urgency than is the case with his whole-time research colleagues. The practitioner cannot thrust problems aside merely because they are insoluble. He cannot discard speculation because it is not susceptible to experiment. Every case he sees of motor neurone disease or disseminated sclerosis must become for the moment a personal issue wherein he has to acknowledge defeat. He is very often made to feel very uncomfortable.

Practitioners' Handicaps

In so far, then, as the impetus to research may be derived from external stimuli, the practising physician has no handicap, but he has others. First, he lacks time for quiet thought. This was what Sir Thomas Browne (1646) felt when he wrote that his work had been composed by snatches of time from his practice, envying those whose "quiet doors and unmolested hours afford no such distractions." The right man, you

*The Harveian Oration delivered at the Royal College of Physicians of London on October 18, 1954.

may say, will make time, but in the press of sessions, practice, and committees this is difficult, and is made no easier by the social conditions of our present days. I believe it right that time should be given to the consulting physician for thought, and that under present conditions it should be given by the State in the sense that some of the time he spends at his hospitals should be allowed for study and research. Provision for this has been made under the National Health Service, and it is to be hoped that the boards and committees of hospitals will make full use of their opportunity in this direction. Looking back myself, I can see how much I might have gained from an hour or two spent each week at hospital making notes of particular cases, for my own use. There is need also for a place for study, and I hope that in the building plans of our new hospitals rooms will be provided adjacent to the wards for the use of the physicians.

The second handicap carried by the practising physician is lack of training in methods of laboratory investigation. Time was when no more was necessary for research than the use of the five senses. Thomas Willis discovered diabetes mellitus from the observation that among those who had frequency of micturition, or what was then called the "Pissing Evil," there was a group who wasted and died, and that in them all the urine was wonderfully sweet to the taste. Discoveries of fundamental importance may still be made without recourse to the laboratory. In our own time one of the most remarkable has been the proof that what we knew as sciatica is almost invariably caused by intervertebral disk disease. It is, however, generally true that a man who would do research in these days must augment the scope of his senses by using an ever-increasing number of technical devices, the mastery of which itself consumes the months. There is no adequate provision for such training in our plan for the education of the consulting physician, but it would surely not be impossible to include a year for the senior registrar in a laboratory where he could learn the rudiments of at least one technical method of investigation, and if such experience came to be generally regarded as of advantage to the candidate for staff appointment the best men would naturally be attracted.

On the other side I would suggest that some at least of the senior appointments in full-time clinical research should be given to men who have been engaged in consulting practice. If a man had before going into practice worked long enough in a laboratory to have learned its methods he would return to it with a mind enlarged and refreshed and, what is perhaps more to the point, with enough unanswered questions to keep him busy for a long time. I believe that among those engaged in consulting practice there would be some who at the end of five years would turn with enthusiasm to whole-time research employment. Some interchange of the kind suggested seems needed to bridge the gap between practitioner and clinical research worker which now exists, to the detriment, I believe, of both parties.

Thomas Willis

Thomas Willis, born forty-three years after Harvey, was a physician who managed to combine research with a busy private practice. Willis was elected a Fellow of the College in 1664 at the age of 43. He had had an unusual career. Born at Great Bedwyn, Wiltshire, he became at the age of 15 batler to a Canon of Christ Church, Oxford, and subsequently took his B.A. On the death of his father and at the outbreak of the Civil War he went to his home at North Hinksey, but we are told by his brother-in-law, John Fell (Willis, 1684b) that, being "harased by the incursions of the Rebels, who were possessed of a Garrison strong enough Five miles from thence, and every where Plundering, he betook himself again to Oxford, being the Tents of the King as well as the Muses; where listing himself a souldier in the University Legions, he received Pay for some years, until the Cause of the Best Prince being overcome, Cromwell's tyranny afforded to this wretched nation a peace more cruel than any war." Soon after the end of the war Willis took his Bachelor of Medicine degree, and we are informed by his contemporary, Anthony Wood (1813–20), that he then "fell to the practice of it and every Monday kept Abingdon market." Thenceforward he became a busy practitioner and remained so until the end of his life, though for six years he combined with this the office of Sedleian Professor of Natural Philosophy at Oxford before moving to London in 1666. And there, Wood tells us, "in very short time after he became so noted, and so infinitely resorted to, for his practice, that never any physician before went beyond him or got more money yearly than he." He died of pneumonia in his house in St. Martin's Lane in November, 1675, and was buried in Westminster Abbey.

During the early years of his practice in Oxford Willis was one of a dozen learned men, four of them physicians, who met regularly for discussion. This was an offshoot of the invisible college, a name given by Robert Boyle to a group who before the war used to meet weekly for philosophic discourse at a London tavern. When the war broke out they split, those remaining in London meeting as before, and those at Oxford in rooms at Wadham. Some time before 1659 the meetings ceased in Oxford and were continued in London, and out of this association was born the Royal Society, of which Willis was one of the original Fellows.

Interesting Conclusions

Willis is, of course, best known for his studies of cerebral anatomy, but, besides being the first person to recognize diabetes mellitus, he was led by his reasoning from clinical observation to certain other interesting conclusions. He was, I believe, the first to envisage a hormone, arguing that "about the time of ripe age as the blood pours forth something through the Spermatic Arteries to the Genitals so also it receives a certain ferment from those parts through the veins: to wit, certain particles imbued with a seminal tincture are carried back into the blood which make it vigorous and inspire into it a new and lively virtue. Wherefore at that time . . . hairs break out, the voice becomes greater, the courses of women flow," and so on. He wrote much on epilepsy and introduced the idea of an explosion in the brain as the cause of seizures, using the analogy of gunpowder. He opposed the current view that the origin of what we call focal seizures lay in the part in which the spasm or sensation appeared, and declared his opinion that the primary cause was always in the brain, "to wit that the spirits inhabiting it being disposed to explosions, and there being exploded, bring on or cause every Falling Evil"; though he thought a peripheral stimulus might excite the explosion.

He wrote well of migraine and gives us an excellent description of this malady in the case of Lady Conway, whose letters (Nicolson, 1930) leave no doubt that she found in him a better doctor than Harvey, who had previously attended her.

In his dissertation "Of the Palsie" he describes clearly the disease we now know as myasthenia gravis, observing it to be distinct from all other kinds of paralysis on account of the variability of its occurrence and the effects of fatigue. Patients with this affliction, he says, may appear well in the morning, "able to walk firmly, to fling about their arms hither and thither, or to take up any heavy thing; before noon . . . they are scarce able to move Hand or Foot." And he goes on to quote the case of a patient under his care, "a prudent and honest woman, who for many years

hath been afflicted by this sort of spurious palsy, not only in her members but in her tongue : she for some time can speak freely and readily enough, but after she hath spoken long, or hastily or eagerly, she is not able to speak a word but becomes mute as a Fish, nor can she recover the use of her voice under an hour or two."

Of his methods he wrote thus : "After I had not found in Books what might satisfy a mind desirous of Truth, I resolved with myself to reach into living and breathing examples: and therefore sitting oftentimes by the Sick, I was wont carefully to search out their cases, to weigh all the symptoms, and to put them, with exact Diaries of the Diseases, into writing ; then diligently to meditate on these ; and then began to adapt general Notions from particular events. . . ." He was first and foremost a clinician, but he was also a fine anatomist, who made great and lasting contributions to the advance of knowledge, especially of the structure of the brain and lungs, their value being enhanced by the beautiful drawings of Christopher Wren.

Association with Lower

In his work on the brain Willis was ably assisted by Richard Lower, who was later to earn fame for his work on the heart and the first blood transfusion. Lower was a younger man than Willis, and afterwards succeeded him in his practice. Wood, in his biographical sketches of the two men, suggests that Lower received too little credit for his contributions to the success of his senior. Willis, for example, was credited with the discovery of a spa, doubtless to the benefit of his practice. But Wood (1813–20) writes that in April, 1664, Lower in his travels with Dr. Willis "made a discovery of the medicinal water at East Throp . . . in Northamptonshire, the doctor being then, as usually, asleep or in a sleepy conditjon on horseback." Afterwards he says Lower imparted his discovery to the doctor, who claimed it for his own. Whatever may be the truth about East Throp, Willis (Franklin, 1931), in his introduction to *Cerebri Anatome*, pays handsome tribute to Lower, "a doctor," he says, "of outstanding learning and an anatomist of supreme skill. The sharpness of his scalpel and of his intellect, I readily acknowledge, enabled me to investigate better both the structure and the function of bodies, whose secrets were previously concealed." And later he writes: "When we were entering upon a much more difficult task, the dissection of the nerves, the really wonderful dexterity of this worker and his untiring perseverance were conspicuous in the extreme and no obstacle could withstand his effort."

Wood, however, could not let this pass, and, writing of Lower, tells us that after taking his degree at Christ Church he "entered upon the physic line, and practised that faculty under Dr. Tho. Willis, whom he helped, or rather instructed. in some parts of anatomy, especially when he was meditating his book *Cerebri Anatome*," and in his list of Willis's published works (Wood, 1813–20) adds under *Cerebri Anatome* this sentence, "Whatsoever is anatomical in that book, the glory thereof belongs to the said R. Lower, whose indefatigable industry at Oxon produced that elaborate piece." Lower himself does not appear ever to have complained that he was not given his due, and his first published work was a spirited defence of Willis's treatise on fevers against the critics, which, as Fulton (1935) has observed, is testimony of the harmonious relations between the two men. Why, then, did Wood write as he did ?

Biased Opinions

Anthony Wood, who would have liked to earn fame as a historian, lived in Oxford from 1632 to 1695. His most notable work was the publication, under the title *Athenae Oxonienses* (Wood, 1813–20), of short biographies of distinguished Oxford graduates up to his time. In these his love for gossip so far outran his discretion that a copy of the second volume of the *Athenae* was burned in public by order of the Vice-Chancellor, and the author was expelled from the University. The book, however, was well received in Cambridge. Wood also kept voluminous diaries (Wood, 1891–1900), which give an entertaining account of his life and times and reveal him as a prejudiced and quarrelsome man. John Fell. the great Dean of Christ Church and later Vice-Chancellor and Bishop of Oxford, who has already been mentioned as the brother-in-law of Willis, was at the same time Wood's benefactor and one of the targets for his abuse. Fell paid for the printing of some of his books, and claimed the right to edit them. Wood could not accept criticism, grumbled, and quarrelled with him.

Richard Lower appears from the diaries to have been one of Wood's intimate friends. During the years 1658 to 1662 Lower's name appears frequently as a companion in the taverns of Oxford. The entries begin with the mention of Mr. Lower, who later becomes Mr. Richard Lower until July 28, 1660, when the entry reads "Spent on Dick Lower at the Mermaid Tavern one shilling." Of Thomas Willis there is no mention in the diaries until 1664, when there is a note of the discovery—by Lower—of the healing well at East Throp. The omission is curious, for Willis was not a negligible person, and it is hardly to be supposed that in a city the size of Oxford the two men never met. That they must in fact have been known to one another is proved by a passage in a letter written in 1725 by Browne Willis, Thomas's grandson, to Bishop Kennett, and preserved in the Bishop's copy of the *Athenae*.

Browne Willis was a scholar and antiquarian of repute, and the purpose of his letter was to refute the statement made by Wood in the *Athenae* that Thomas Willis's grandfather was a tailor. This letter begins, "I most readily obey your lordshipp's commands in communicating something of my good grandfather Dr. Willis. A. Wood, who was his next neighbour in St. John Baptist's parish Oxon, and had a disagreement with the family, says several things untrue of his descent." From these observations it seems likely that Wood had a prejudice against Willis and a favourable inclination towards Lower, and it is certain that as a historian he would have been influenced by whatever prejudices he may have had.

There is, moreover, evidence that Wood's account of the relative contributions of Willis and Lower to *Cerebri Anatome* was derived from a source already biased. Henry Stubbe, philosopher and physician, published (Stubbe, 1670) a series of papers the sole object of which was to discredit the Fellows of the Royal Society (whom he called contemptuously the Virtuosi), and he attacked Willis among others. He alleges that Willis could not have spared the time from his great practice to compose *Cerebri Anatome*, and writes, "Whatsoever there is in that Piece, which is Anatomical, the glory thereof belongs to Dr. Lower, whose indefatigable industry produced that elaborate Treatise" (p. 95). We know from Wood's diary that he had purchased Stubbe's book, and his comment in the *Athenae*, published many years later, is an almost exact transcription of the sentence I have just quoted ; but what he ignored, or perhaps had never read, was a postscript. This is to be found out of its context at the end of Stubbe's little volume. It begins "I think myself obliged to adde one thing more where I speak as if Dr. Willis had had little to do in the discoveries of Dr. Lower about anatomy," and goes on to say that, although Lower did the dissections, Willis's was the master mind which inspired and directed the work. The last sentence of this recantation is revealing: "Thus much I thought fitting to annex, lest the Virtuosi should censure me as partial to my old School-fellow, Dr. Lower, or swayed by any regard then that of Truth" (p. 178).

It is due to Willis that this story should be told in full, for some of those who have written about him have followed Wood, including Michael Foster (1901), who tells us that Lower was "the henchman of the fashionable Willis whose false fame in large measure rested on Lower's careful, unacknowledged work." In this I scent something of the odour in which the physiologist held the successful practitioner 50 years ago.

Willis's "Cerebri Anatome"

Cerebri Anatome was published in 1664 and is chiefly distinguished for the description of the cranial nerves, but better known for the dissertation upon the arteries at the base of the brain. Wren's drawing shows the anterior cerebral arteries joining where the anterior communicating artery should be and bifurcating a little further forward, but, apart from this, there is no fault. Willis, however, saw that there was a circle and that it must have some physiological significance. In discussing this he first suggests that the function of the circle is to mix the blood before its distribution to the brain, but on a later page adds:

"But there is another reason far greater than this of these manifold ingraftings of the Vessels, to wit, that there may be a manifold way, and that more certain, for the blood about to go into divers Regions of the Brain, laid open for each; so that if by chance one or two should be stopt, there might easily be found another passage instead of them: as for example, if the Caroüd of one side should be obstructed, then the Vessels of the other side might provide for either Province. . . . Further, if both the Carotids should be stopt, the offices of each might be supplied through the Vertebrals" (Willis, 1684a).

He goes on to say:

"It is not long since we dissected the dead body of a certain man, whom a great Scirrhus or hard Swelling within the Mesentery, growing at last ulcerous, had killed. When his Skull was opened, we beheld those things belonging to the Head, and found the right Carotid, rising within the Skull plainly bony or rather stony, its cavity being almost wholly shut up; so that the influx of the blood being denied by this passage, it seemed wonderful, wherefore this sick person had not dyed before of an Apoplexy: which indeed he was so far from, that he enjoyed to the last moment of his life, the free exercise of his mind and animal function . . . This Gentleman, about the beginning of his sickness, was tormented with a cruel pain of the Head towards the left side. The cause whereof I know not how better to explain, than that the blood excluded from the right Carotid Artery, when at first it rushed more impetuously in the left, had distended the Membrane" (Willis, 1684a).

Dissertations on the Circle

It is perhaps remarkable that Willis nearly three hundred years ago asked himself why this man did not have a hemiplegia, and perceived from his dissections of the circle that anatomy might supply the answer, but it is even more to his credit that he should have remembered the episode of headache and found what was probably the correct explanation for it. Willis was an indefatigable student of symptoms. This is apparent in the case histories illustrating his clinical writings, and when he was at his dissections he was ever thinking not only of the function of the structures he laid bare but of the disorder of function that might result from their disease. This, you may say, is the way any liberal-minded anatomist thinks, but Willis was a busy practitioner, able to draw upon his own experience of symptoms unexplained. We may be sure that he would have been interested in what we now think about the functions of his circle, and the symptoms that occur when one of the internal carotid arteries is occluded. His observation that this may happen without hemiplegia has, of course, been amply confirmed, and also the appearance of headache as a symptom of the event. That it may be the only symptom we know from an example in which headache in a young woman without other symptoms was investigated by arteriography and internal carotid occlusion demonstrated; and in patients with hemiplegia headache as a preliminary symptom is not uncommon. The explanation we believe to be correct is that which occurred to Willis—distension of other vessels—for we know that when the wall of an artery of the head is stretched beyond physiological limits headache results.

Recent Experimental Work

As to what happens in the circle after occlusion we can only speculate, but our speculations may be guided by methods of observation and experimental records which were not available to Willis. The experiments in which he would have delighted most are those in which a dye or other visible substance is injected into one of the afferent arteries of the circle, for such experiments he performed himself in the cadaver. Cerebral arteriography has now enabled us to see in man the course of radio-opaque solutions injected into the internal carotid and vertebral arteries, both in the normal state of the circulation and when one or both internal carotids are occluded. What we see in the arteriograms cannot be an accurate picture, for the opaque solution is injected under pressure, but arteriography has taught us a great deal. Provided that the anterior communicating artery is of fair calibre, fluid injected into one internal carotid artery, when the other is occluded by digital compression, flows into both hemispheres, and if there is bilateral carotid occlusion proximal to the circle a vertebral injection enters the branches of the internal carotid arteries by way of the posterior communicating branches, as Willis imagined.

A way of learning what happens in the normal circle is to watch the flow of injected dye in a living animal, the brain being exposed by operation. This had been done before, but not with the essential precaution of introducing the solution of dye into a vertebral or carotid artery without disturbing the normal pressure. McDonald and Potter (1951), observing this precaution, have shown that the dye entering a vertebral artery flows into the basilar and posterior cerebral arteries and forward into each posterior communicating artery up to a point about midway along its length. Conversely, dye injected into a carotid artery passes into the anterior and middle cerebral arteries of that side and the anterior cerebral artery, and backwards into the posterior communicating artery up to a point halfway along its length. At this point injection into either the vertebral or the carotid artery results in an interface of blood and dye, a dead point, at which the pressure of the two opposing streams is balanced. There is in fact no flow of blood through the posterior communicating arteries at all.

In the rabbit, which was used for these experiments; there is a single anterior cerebral artery and therefore no anterior communicating artery, but, having regard to the observation that in man a radio-opaque solution injected into one internal carotid ordinarily fills only the anterior cerebral of the same side, it is probable that in the normal circle of Willis there is another dead point at the mid-point of the anterior communicating artery. Thus there are virtually three separate streams of arterial blood supplying the brain, one from the basilar and one from each internal carotid artery, separated from one another not by any physical barrier, but by the dead points in the posterior and anterior communicating arteries, the position of each of these dead points depending upon the balance of pressure in the opposing streams.

Internal Carotid Occlusion

The most frequent cause of internal carotid occlusion is atherosclerosis, and the site is usually in the neck within a centimetre of the origin of the artery. Before the advent of total obstruction there must be a gradual narrowing of the lumen, which favours the establishment of collateral circulation. We may compare this with what happens when there is atherosclerosis of a coronary artery, for in the heart as in the brain occlusion may occur without infarction if the process of narrowing is slow and there is time for a good collateral circulation to develop. In the brain there is opportunity for widening of anastomotic channels between the superficial branches of the posterior and middle cerebral arteries, and, as we know from arteriography, the communication in the orbit between branches of the external carotid and the ophthalmic branch of the internal carotid can short-circuit the obstruction in the neck. The direction of flow in the ophthalmic artery being then reversed, it receives blood from the external carotid which, entering the lumen of the internal carotid above the obstruction, fills the middle cerebral artery. But the circle of Willis must

provide the most important source of compensatory flow. When pressure falls on the obstructed side there must be a shift of the dead point in the anterior communicating artery and a flow of blood from the unobstructed side to fill the anterior and probably the middle cerebral arteries on the obstructed side. Both hemispheres must then obtain their main blood supply from the unobstructed internal carotid, which, being in a part of its course enclosed within a bony canal, cannot be capable of any great dilatation, though even a small increase in its diameter would be an important contribution, since the volume of fluid passing through a tube varies with the fourth power of its radius. It is probable that under these conditions the maintenance of cerebral blood flow in patients who do not develop hemiplegia as an immediate effect of carotid occlusion depends mainly upon a rise of mean arterial blood pressure, for this has been observed as an effect of carotid ligation.

The equitable distribution of blood to the two hemispheres after occlusion of one internal carotid artery requires an anterior communicating artery of adequate diameter, but it seems probable that alterations of calibre in the peripheral vessels of the two hemispheres must play a part. The local effect of cerebral ischaemia is vasodilatation from the accumulation of CO_2. The hemisphere on the obstructed side, therefore, at any rate for a time, may claim more than an equal share of blood with a corresponding vasoconstriction in the hemisphere on the unobstructed side. This surmise finds support in the observation immediately after common carotid ligation of abnormal waves in the electroencephalogram in both hemispheres and occasionally only in that supplied by the unobstructed artery (P. Schurr, personal communication). If after internal carotid occlusion by disease, the total cerebral blood flow is at times less than normal and the hemisphere on the obstructed side simultaneously demands more than its fair share, this might explain the occurrence of transient loss of function in the limbs on the ipsilateral or obstructed side of the body in certain cases.

Compensatory Mechanisms

When cerebral function remains intact after internal carotid occlusion we may assume that the various compensatory mechanisms have come into action, but the situation must still be precarious. The haemodynamic crisis that has occurred is not a transient affair. There is a perpetual struggle both for the maintenance of the total cerebral blood flow and for its equitable distribution; and loss of blood volume, a fall of blood pressure, or a temporary upset of the balance between vasoconstriction and vasodilatation may cause local ischaemia or infarction with reversible or irreversible loss of function. An irreversible hemiplegia is the commonest ending, and is indeed often the first event, but it is the preliminary symptoms occurring in certain cases which invite explanation. Headache, as Willis first observed, may be one. Hemiplegia may be preceded by episodes of weakness or numbness over a period which may extend from a few hours to several years. The loss of function in these episodes may be severe, with rapid and complete recovery, and this may recur so often that occlusion of peripheral branches, by extension of clot from the site of the original obstruction, or by detached emboli, can hardly explain them. I suggest that this episodic loss of function, which must be ischaemic, is not due to any fresh vascular obstruction, but to a temporary failure of the compensatory mechanisms.

I shall venture, following the example of Willis, to relate some particulars of a patient in whom the brain was finally inspected.

This patient was a woman aged 53, known to have had mitral stenosis with auricular fibrillation for several years. The first symptom of cerebral disorder was headache, which had begun to trouble her three years previously. Its first onset was sudden, and thereafter it occurred almost daily for several hours and continued thus for six months, after which it became much less frequent and severe. Eighteen months before I saw her she had transient loss of vision in the right eye, shortly followed by numbness and weakness of the right limbs with recovery in 24 hours. A month later there was another episode of transient right hemiparesis. A few days after she had recovered from this she had a left hemiparesis, from which recovery was complete in 48 hours. From this time onwards she had frequent attacks of a similar nature in which sometimes the right limbs were affected, sometimes the left. On the last occasion, six weeks before I saw her, she suddenly found her left hand weak and tremulous and then her right leg. This was accompanied by right-sided headache. Recovery occurred as usual in 24 hours. These episodes had been attributed to cerebral emboli, but when she came to see me in my consulting-room she was active and well, apart from the complaint of general tiredness, and on examination showed no trace of weakness or loss of sensation nor any abnormality of the reflexes apart from a relative briskness of the left arm jerks. She was admitted to hospital a few days later and died from the effects of an embolus in her left internal carotid artery. At the post-mortem inspection the findings relevant to this story were an old organized embolic occlusion in the right internal carotid artery just proximal to the circle of Willis, and two small areas of infarction of old standing, one in each hemisphere in the neighbourhood of the internal capsule.

I suggest that the occlusion of the right internal carotid artery was responsible for the phase of headache, which became less as anastomosis improved. At some time thereafter she had a small embolic infarction in each hemisphere. Each of these lesions could have caused a transient hemiparesis but could not have accounted for the very frequent attacks that have been related. Each, however, may well have resulted in a special local demand for compensatory circulation, and so have added to the effect of temporary failure of the compensatory mechanism as a whole in determining transient weakness and numbness of the limbs.

Only in one other patient have I encountered the story of transient loss of function in the limbs on the same side as the carotid obstruction, a woman who finally developed a left hemiplegia with arteriographic proof of occlusion of the right internal carotid artery in the neck. She had first attended hospital six years previously for attacks which were then regarded as hysterical. They continued up to the time of the hemiplegia. They never occurred except during menstruation, and then quite often. The onset was rapid, with a feeling she described as that of going under ether, and this feeling persisted throughout the attack. The next sensation was that of weakness and numbness experienced in those parts of her body which were in use—the arm or leg on one side of the body, never on both sides, but as often on the right as the left. If she were talking at the onset of an attack indistinct speech would be the first evidence of weakness. The whole episode lasted about five minutes, and with it she would have a bursting sensation in the neck. She had very occasionally lost her senses briefly at the height of the attack. There may be in this case some anomaly of the circle of Willis. I mention it as an example of symptoms which seem to depend upon some recurrent haemodynamic crisis following internal carotid occlusion, for I suppose this existed from the first and that the hemiplegia was the final result of a complete failure of compensation.

A Well-recognized Symptom

Transient blindness on the same side as the obstructed internal carotid is now a well-recognized symptom, though by no means common. These attacks, usually occurring at irregular intervals of days or weeks, are of a fairly constant pattern, of sudden onset and lasting from one to five minutes. As a rule they precede hemiplegia, often by many months, and frequently cease before that event. There is no doubt that the blindness is due to transient retinal ischaemia, for the retinal arteries have been observed in an attack and are bloodless. I suspect this is an example of what may be happening elsewhere in the cerebral circulation, but here with a more impressive clinical effect, for the reason that the retinal arteries have no anastomosis. The cessation of these attacks of blindness some time after internal carotid occlusion may be due to an increase of the flow from the external carotid side as anastomotic channels widen.

Conclusion

I imagine it may have been the lot of more than one Harveian Orator, as he comes to the end of his discourse, to fear that he has disappointed expectation and fallen short in the performance of an honourable duty. I have taken the name of Thomas Willis for commemoration as one of the Benefactors of the College. He gave well of the fruits of his labours preserved in those many pages which even Anthony Wood (1813–20) praised for the "natural smoothness, pure elegancy, [and] delightful, unaffected neatness" of their Latin style. I have occupied some part of your time with speculation about the cause of symptoms resulting from occlusion of the internal carotid artery. If there be anything in this of the least value let me exhort you, as I have the right, to search and study out these secrets of nature by way of experiment. Willis would have approved this exhortation and perhaps have thought us laggards. He foresaw great works. The ancients, he said, bound to false suppositions, might be excused the faulty structure of their reasoning, but "those who come after should take care for the Re-edifying of the Building even from the ground, on which our most famous Harvey hath laid the Circulation of the Blood as a new Foundation in Medicine."

REFERENCES

Anonymous (1830). *Lives of British Physicians*, p. 58. London.
Browne, T. (1646). *Pseudodoxia Epidemica*, preface. London.
Foster, M. (1901). *Lectures on the History of Physiology*, p. 181. Cambridge.
Franklin, K. J. (1931). *Proc. roy. Soc. Med.*, **25**, Sect. Hist. Med., 8.
Fulton, J. F. (1935). *Bibliography of Two Oxford Physiologists*, p. 13. Oxford.
McDonald, D. A., and Potter, J. M. (1951). *J. Physiol. (Lond.)*, **114**, 356.
Nicolson, M. H. (1930). *The Correspondence of Anne, Viscountess Conway*. London.
Schurr, P. Personal communication.
Stubbe, H. (1670). *Legends no Histories; or a Specimen of Some Animadversiones upon the History of the Royal Society*, Pt. 2. London.
Willis, R. (1664). *Cerebri Anatome: cui Accessit Nervorum Descriptio et Usus*. London.
—— (1684a). *Anatomy of the Brain*, p. 68. Published in his *Practice of Physick*. London.
—— (1684b). Introduction to *Pharmaceutice Rationalis*, Pt. 2. Published in his *Practice of Physick*. London.
Wood, A. (1813-20). *Athenae Oxonienses*, 4 vols. London.
—— (1891-1900). *Life and Times of Anthony Wood*, 5 vols. Oxford.

PANCREATITIS FOLLOWING PREGNANCY

BY

R. A. JOSKE,* M.D., M.R.A.C.P.

From the Clinical Research Unit of the Walter and Eliza Hall Institute of Medical Research and the Royal Melbourne Hospital, Victoria, Australia

The relation between pregnancy and pancreatitis is little discussed in the literature, although many reports of pregnancy complicated by pancreatitis have been published (Kingsley, 1934; Cassel and Malewitz, 1950; Burger, 1952) since the cases of Schmitt (1818) and of Lawrence (1831) early last century. Langmade and Edmondson (1951) collected 53 cases from the literature and reported nine more of their own.

The earliest report of pancreatitis occurring in the post-partum period seems to be that of Haidlen (1884). Watts (1918) and Fallis and Plain (1939) have each reported two cases, and others have been described or mentioned by Deaver (1918), Paxton and Payne (1948), Roberts *et al.* (1950), Rose (1951), and Comfort and Steinberg (1952). McWhorter (1932) reported 64 cases of pancreatitis in two of which "the onset of pancreatitis occurred shortly after childbirth." Langmade and Edmondson (1951) noted that, in pancreatitis complicating pregnancy, liability to an exacerbation during the puerperium was an outstanding characteristic.

Nevertheless, most recent writers do not stress pregnancy as an aetiological factor in pancreatitis (Paxton and Payne, 1948; Warren, 1948; Macnab, 1949; Fallis, 1951; Saint and Weiden, 1953). There is, however, increasing evidence to support the idea of Whipple (1907) that "acute" and "chronic" pancreatitis are differing phases of the same disease process (Comfort *et al.*, 1946), while Saint has rightly emphasized that "pancreatitis" is a general term covering several diseases which have in common only the feature of localization to the pancreas (Saint and Weiden, 1953).

This paper reports six patients with pancreatitis, in all of whom the disease was first manifest a few weeks or months after completion of pregnancy, in whom the clinical and laboratory findings were similar, and none of whom presented any evidence of the known causes of pancreatitis. It is suggested that these patients may be representative of one type of pancreatitis which forms a distinctive syndrome, to be separated from the large group of patients with "pancreatitis of unknown aetiology." For convenience, some of the features of these cases are given in Table I.

Case 1

A woman aged 20 was admitted on May 29, 1954. One year before admission she had been delivered of a stillborn child. Six weeks after this she developed flatulent dyspepsia and intermittent epigastric distress, later followed by severe constant epigastric pain radiating through to the back on the left side. She vomited occasionally. The pain was worse after fatty foods. Two weeks before admission she had more severe pain than previously, and this was followed by persistent vomiting and then jaundice with dark urine and pale stools.

On examination she was jaundiced. Her temperature was 99.8° F. (37.7° C.), pulse 80, blood pressure 120/90 mm. Hg. There was rigidity and guarding over her abdomen, but she was more tender in the epigastrium. The liver and gall-bladder were impalpable. The diagnosis of obstructive jaundice due to pancreatitis was made. The urinary diastase level was 400 units.

Laparotomy was performed on June 1. The gall-bladder was normal and contained no calculi, while the pancreas was irregularly enlarged and thickened. The common bile duct was drained and a pancreatic biopsy was performed; this showed pancreatitis (Fig. 1).

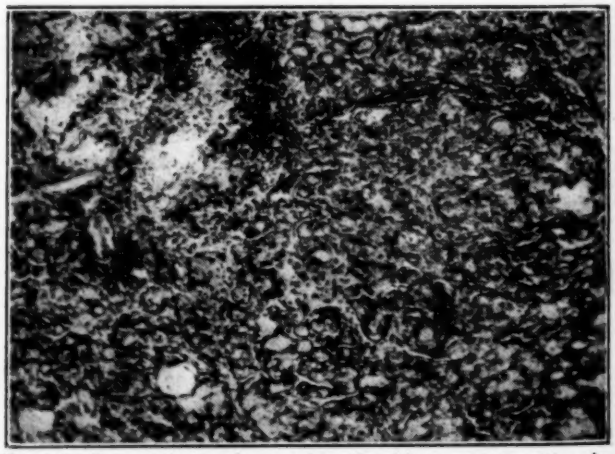


FIG. 1.—Pancreatic specimen taken for biopsy at operation in Case 1. At this stage the patient was still jaundiced and the urinary diastase elevated. The specimen shows increased fibrous tissue and cellular infiltration without necrosis of the parenchymal cells; the pancreatic ducts are slightly dilated. (Van Gieson. ×144.)

*Working with the aid of a grant from the National Health and Medical Research Council of Australia.

TABLE I.—*Some Clinical Features of Six Patients with Post-partum Pancreatitis*

Case No.	Family History	Parity	Pregnancy	Child	Time of Onset of Symptoms after Pregnancy	Time of Onset of Acute Pancreatitis	Abdominal Pain	Vomiting	Jaundice	Gall-stones	Result
1	Aunt had cholelithiasis	1	Normal	Stillborn	6 weeks	12 months	+	+	+	0	Well
2	Nil	1	"	Living	3 months	3 "	+	+	+	+	"
3	"	1	Hypertension induction of labour	"	2 weeks	6 weeks	+	+	+	+	Recurrent pain two years later
4	"	1	Normal	"	9 months	11 months	+	+	0	+	Well. Again pregnant
5	"	1	Some flatulence and vomiting	"	A few days post partum	2 years	+	+	Slight	+	Well
6	Father had cholelithiasis	2	Normal	"	11 weeks	14 weeks	+	+	0	?	?

Her convalescence was uneventful. A cholangiogram through the tube in the common bile duct on June 28 showed the anatomy of the biliary tree to be normal, and the contrast medium entered the duodenum freely (Fig. 4). The tube was removed on June 30. She has remained well since.

Case 2

This patient, aged 23, was first admitted on February 3, 1954. Three months before admission she had a normal delivery after a normal pregnancy. Two days before admission she had a sudden onset of severe colicky pain in the epigastrium radiating through to the back and associated with nausea and persistent vomiting. This was followed next day by jaundice with dark urine and pale faeces.

On examination she was icteric. Her temperature was 99° F. (37.2° C.), pulse 100, blood pressure 125/80 mm. Hg. There was tenderness in the epigastrium. The diagnosis of pancreatitis and cholelithiasis was made, although no urinary diastase estimation was done at this stage. She responded to conservative treatment with pethidine and antibiotics.

A cholecystogram on March 1 showed multiple non-opaque calculi in the gall-bladder. At laparotomy on March 5 the pancreas was enlarged, firm, and nodular. The common bile duct was normal. The gall-bladder was not thickened, but it contained small stones. Cholecystectomy was performed uneventfully. The patient has since remained well.

Case 3

A young woman, aged 19, was first admitted on December 31, 1951. Eight weeks previously she had been successfully delivered of her first child after a pregnancy complicated by hypertension and terminated by medical induction of labour. Two weeks later she had developed sudden severe pain in the back, followed by two milder attacks. Four days before admission she had a fourth attack, more severe than the earlier ones, felt both in the back and in the epigastrium and associated with vomiting. Her urine was dark and her faeces were pale.

On examination she was icteric; temperature 99° F., (37.2° C.), pulse 96, blood pressure 140/80 mm. Hg. She was thought to have cholelithiasis, and a cholecystogram on January 14, 1952, showed multiple radiolucent calculi. At operation on January 17 the gall-bladder was thickened and contained calculi. Cholecystectomy was performed. The pancreas was not examined. Convalescence was delayed by a wound infection producing erythema nodosum and necessitating secondary suture. She was discharged on March 1.

When seen again on January 28, 1954, she complained of flatulent dyspepsia and recurrent severe abdominal pain radiating through to the back and with occasional vomiting. The attacks had occurred every two or three weeks for some months. She had noted no jaundice. The clinical diagnosis of relapsing pancreatitis was confirmed by a urinary diastase of 160 units on January 28. She has been treated with a low-fat diet and atropine and ephedrine orally, with decrease in the frequency and severity of her pain.

Case 4

A woman aged 22 was admitted on March 22, 1954. Two months before admission, and nine months after a normal pregnancy, she developed flatulent dyspepsia and recurrent epigastric pain radiating through to the back, associated with vomiting and a dark coloration of her urine. Three days before admission she had severe persistent pain in the left upper quadrant of her abdomen radiating to the back, and frequent vomiting.

On examination she was not jaundiced. Her temperature was 101° F. (38.3° C.), pulse 100, blood pressure 140/90 mm. Hg. There was tenderness and rigidity in the upper abdomen, more marked on the left side. A clinical diagnosis of pancreatitis was confirmed by a urinary diastase estimation of over 2,000 units. She responded to conservative treatment with gastric aspiration, intravenous fluid replacement, pethidine, and antibiotics.

Oral cholecystography on April 7 failed to outline the gall-bladder, but an intravenous choledochogram on May 20 showed a large gall-bladder containing multiple stones up to 1 cm. in diameter.

Laparotomy was performed on June 4. An operative cholangiogram showed the dye medium to enter the duodenum freely. There was no evidence of residual pancreatitis. The common bile duct was normal. The gall-bladder contained multiple stones and was removed, and a pancreatic biopsy was done (see below). The patient has remained well since operation, although she is again pregnant.

Case 5

A woman aged 26 was first admitted on March 22, 1949. Two years previously, a few days after childbirth, she developed epigastric pain and flatulence lasting a few days and recurring thereafter at intervals of weeks. Six days before admission she had sudden severe epigastric pain radiating through to the back and associated with nausea and vomiting.

On examination she was acutely ill and slightly icteric. Her temperature was 100.6° F. (38.1° C.), pulse 120, blood pressure 150/100 mm. Hg. Epigastric tenderness and rigidity were present. The diagnosis of acute pancreatitis was confirmed by a urinary diastase level of over 1,000 units. She was treated conservatively with morphine and antibiotics, and gradually improved over the following week.

A cholecystogram on April 8 showed multiple small calculi in the gall-bladder, and laparotomy was performed on May 4. There was fat necrosis in the omentum and mesocolon; the pancreas was thickened and irregular; the gall-bladder was thickened and contained calculi, but the common bile duct was normal. Cholecystectomy was performed uneventfully.

When last seen twelve months after operation she was well and free of pain and dyspepsia.

Case 6

A woman aged 22 was admitted on March 17, 1954. Fourteen weeks previously she had completed a normal pregnancy. Three weeks before admission she had a mild attack of epigastric pain lasting two days. Two days before admission she had sudden onset of severe constant epigastric pain radiating to both flanks, with nausea and vomiting.

On examination she appeared flushed and drawn, but was not jaundiced. Her temperature was 100.6° F. (38.1° C.), pulse 136, blood pressure 130/90 mm. Hg. Her abdomen was slightly distended, with generalized tenderness, and there was guarding in the epigastrium.

A urinary diastase estimation of 2,000 units confirmed the clinical diagnosis of pancreatitis. Conservative treatment with intravenous therapy, pethidine, and antibiotics resulted in rapid improvement in her condition, and she was discharged on March 31. No follow-up studies have yet been possible on this patient.

Laboratory Investigations

The laboratory investigations in all patients followed a similar pattern, and may conveniently be considered together (Tables II and III).

TABLE II.—*Salient Laboratory Findings in Six Cases of Post-partum Pancreatitis. In Cases 2 and 3 the Urinary Diastase Estimations were Made After recovery from the Acute Stage of the Disease*

Case No.	Urine				Blood		Total Serum Lipides (mg./100 ml.)	Serum Cholesterol (mg./100 ml.)
	Proteinuria	Glucosuria	Bile	Diastase	Hb (g.%)	Leucocytes (per c.mm.)		
1	+	+	+	400	13·3	6,000	480	160
2	0	0	+	30	12·1	7,000	520	210
3	0	0	+	160	11·3	11,200	500	195
4	0	+	+	2,000	9·9	16,000	500	—
5	+	0	+	1,000	14·0	28,800	—	—
6	0	0	+	2,000	7·8	15,000	—	—

TABLE III.—*Liver-function Tests in Six Cases of Post-partum Pancreatitis. The Significant Abnormalities are slight Elevation of the Serum Bilirubin and Alkaline Phosphatase in Cases 1, 3, 4, and 5*

Case No.	Serum Bilirubin (mg./100 ml.)	Cephalin Flocculation	Serum Albumin (g. %)	Serum Globulin (g. %)	Serum Gamma Globulin (g. %)	Serum Alkaline Phosphatase (K–A Units)
1	4·0	Weak positive	4·7	2·0	0·8	23
2	0·2	Negative	4·5	2·3	0·9	7
3	0·2	"	5·6	2·1	1·3	29
4	2·5	Weak positive	4·3	1·9	0·9	12
5	6·0	Negative	4·8	2·3	—	25
6	0·5	Weak positive	3·7	2·0	—	—

Urine Examination.—Two patients (Cases 1 and 5) showed transient proteinuria, two (Cases 1 and 4) transient glucosuria, and all cases had bile in the urine during the acute stage of the disease (Table II). In all cases examination of the urine was normal on discharge from hospital.

Urinary Diastase.—In four patients estimations of the urinary diastase level on admission to hospital with severe symptoms revealed diagnostic levels confirming the clinical diagnosis of pancreatitis (Table II). In Case 3 a less marked elevation to 160 units was recorded when the patient presented with post-cholecystectomy dyspepsia three years after the attack of "acute cholecystitis." This reading is regarded as diagnostic in this laboratory. In Case 2 no significant elevation of the urinary diastase was found, but it was not possible to examine the urine during an exacerbation of symptoms. In this patient the diagnosis of pancreatitis was confirmed at laparotomy. Serum amylase levels were not investigated.

Blood Examination.—The results of blood examinations were variable. Two patients had a moderate hypochromic anaemia. Acute exacerbations were accompanied by a polymorphonuclear leucocytosis, which in Case 5 reached 28,800 per c.mm. (Table II).

Liver-function Tests.—The results of liver-function tests are detailed in Table III. They show slight elevation of the serum bilirubin and alkaline phosphatase, without change in plasma protein levels. When symptoms were severe a weakly positive cephalin flocculation was sometimes noted. The findings suggest that jaundice in these patients is obstructive in type, although slight hepatocellular damage may accompany peritoneal irritation in exacerbations of the disease. None of these patients was subjected to liver biopsy.

Gastric Investigations.—Because of the frequency with which the patients complained of flatulent dyspepsia, a histamine test-meal examination was made in five cases (Cases 1, 2, 3, 4, and 5), and in all it revealed a normal gastric acidity. Gastric biopsy in Cases 1 and 4 by the method of Wood *et al.* (1949) showed normal mucosa in both.

Glucose-tolerance Tests.—Oral glucose-tolerance tests after 50 g. of glucose were performed on three patients (Cases 1, 2, and 4), and none had hyperglycaemia or a diabetic type of curve.

Serum Lipide and Cholesterol Levels.—There was no elevation of the total serum lipides measured by the turbidimetric method of Kunkel *et al.* (1948) or of the serum cholesterol in those cases in which they were measured (Table II). In Cases 2, 3, and 4 fat-tolerance curves after ingestion of 50 g. of butter were performed after recovery from the acute stage. In all three cases these suggested poor absorption, consistent with impaired pancreatic function (Fig. 2).

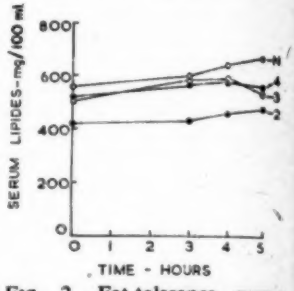


FIG. 2.—Fat-tolerance curves in Cases 2, 3, and 4. In all there is a low fasting lipide level and a rise of less than 100 mg. per 100 ml. after 50 g. of butter orally.

Other Investigations.—The intravenous secretin test was not used in this study, as in our hands it has produced results too variable to be of great diagnostic value. Similar variations have been reported from other centres (Dornberger *et al.*, 1948; Heffernon and Gunter, 1951). In all patients the Wassermann reaction was negative. The erythrocyte sedimentation rate was raised during exacerbations of symptoms.

Radiological Studies

Plain *x*-ray films of the abdomen and chest were normal in all cases.

Oral cholecystography was performed in Cases 2 to 5 after recovery from the initial "acute pancreatitis," an interval of about three weeks. In Cases 2, 3, and 5 this revealed multiple small non-opaque calculi in the gall-bladder. However, in Case 4 there was no radiological demonstration of the gall-bladder, and an intravenous choledochogram was done six weeks later, eight weeks after initial admission to hospital. This showed the gall-bladder to be enlarged and to contain multiple calculi; the bile ducts were not outlined.

A cholangiogram was performed at operation in Case 4 (Hughes and Kernutt, 1954b). There was good filling of the biliary tree. The contrast medium flowed freely into the duodenum, and there was no demonstrable abnormality at the lower end of the common bile duct. In one film the medium had entered the main pancreatic duct by retrograde flow, and no obstruction to this was noted (Fig. 3).

In Case 1 a cholangiogram was performed four weeks after operation before removal of the T-tube from the common bile duct. The medium entered the duodenum freely and the common bile duct was normal, with the usual anatomical tapering at the lower end (Hughes and Kernutt, 1954a). No evidence of cholelithiasis was obtained (Fig. 4).

Pancreatic Biopsies

Biopsy of a specimen from the body of the pancreas was obtained at operation in Cases 1 and 4. There were no adverse sequelae from these procedures.

In Case 1 the biopsy was carried out a year after completion of pregnancy and three weeks after the onset of jaundice, at a time when the urinary diastase was still slightly raised. This biopsy showed slight increase in fibrous tissue, distorting the normal pancreatic architecture. There was some infiltration by fibroblasts, lymphocytes, and polymorphs. The acini were slightly irregular but without areas of necrosis of the parenchymal cells (Fig. 1).

The biopsy in Case 4 was carried out twelve months after the birth of her child and five months after she first developed dyspepsia. At the time of operation she had been free of symptoms for two months. The biopsy showed normal pancreatic tissue, without evidence of the preceding inflammation and with no residual fibrosis or fatty infiltration.

Discussion

These patients, and those reported by other authors, have many features in common. All were young women who developed flatulence and recurrent bouts of abdominal pain and vomiting within a few days or weeks of pregnancy, culminating in an attack of "acute pancreatitis." In all of them the clinical and laboratory findings were closely similar.

The aetiology of the pancreatitis is of the greatest interest. None of the six patients presented clinical or epidemiological evidence of infection with mumps or the other viruses known occasionally to cause pancreatitis. All had excellent dietetic histories, with no suggestion of alcoholism or malnutrition. In only two of the six was there a family history of cholelithiasis; none had a family history of cardiovascular disease, xanthomatosis, diabetes mellitus, or pancreatitis, and in four cases estimations of serum lipide and cholesterol levels revealed normal values (Table II; Fig. 2). One patient (Case 2) has a binovular twin who has borne two children without evidence of pancreatic disease. These facts render unlikely the hereditary type of pancreatitis recently described and associated frequently with hyperlipaemia (Holt *et al.*, 1939; Collett and Kennedy, 1948; Comfort and Steinberg, 1952; Klatskin and Gordon, 1952). It should nevertheless be noted that one patient (No. II 3) in the family reported by Comfort and Steinberg (1952) first developed symptoms a month after the birth of her first child.

FIG. 4.—Post-operative cholangiogram in post-partum pancreatitis (Case 1). The arrangement and calibre of the bile ducts are normal, and the contrast medium enters the duodenum freely. There has been some retrograde filling of the main pancreatic duct.

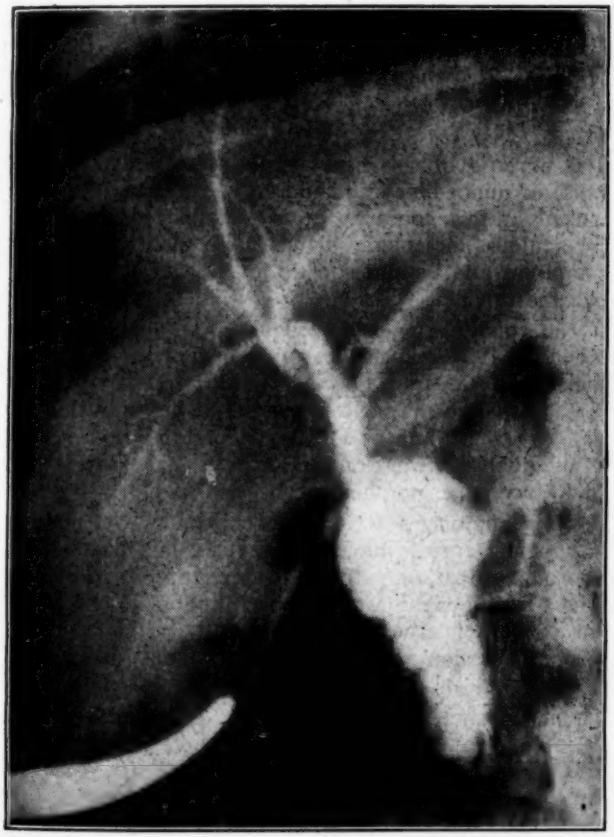


FIG. 3.—Operative cholangiogram in pancreatitis following pregnancy (Case 4). There is no biliary obstruction and the anatomy of the bile ducts appears normal. There has been some filling of the main pancreatic duct.

The relation between the pancreatic lesions and cholelithiasis must also be considered. Cholelithiasis was present in four of the five cases in which full radiological studies and laparotomy were performed, but in none were stones found in the common bile duct, and in none was any abnormality of the sphincter of Oddi demonstrated. In Cases 1 and 4 cholangiography showed the duct of Wirsung to be freely patent (Figs. 2 and 3). Langmade and Edmondson (1951) in their survey of 53 reported cases of pancreatitis complicating pregnancy found 34 in which the gall-bladder was examined at operation or after death, but calculi were noted in only 12 of these. They stated that "there was no particular difference between those with and those without [gall-stones] as far as the onset and course of their pancreatitis was concerned." There is also statistical evidence to suggest that there is little direct relation between pregnancy and cholelithiasis (Gross, 1929; Joske *et al.*, 1954). For these reasons it is thought improbable that cholelithiasis in these patients has any aetiological significance, but rather that biliary stasis due to pancreatitis may be responsible for the development of cholelithiasis, or that both cholelithiasis and pancreatitis are sequelae of the lipaemia of pregnancy.

Reflux filling of the main pancreatic duct was shown radiologically in two patients (Cases 1 and 4). The work

of Hicken and McAllister (1952) suggests strongly that reflux into the main pancreatic duct is a frequent and normal finding in man, and of no pathological significance. They found also that this reflux may occur whether or not there is a common entry of the common bile and pancreatic ducts into the duodenum. Experience with cholangiography in this hospital agrees with this (Hughes and Kernutt, 1954b), and the relation of biliary reflux to pancreatitis in man is thought to be slight.

It is therefore postulated that these patients were in fact suffering from a type of chronic relapsing pancreatitis which is in some way related to pregnancy, and that this may represent an entity within the large group of diseases considered together as "pancreatitis."

The abnormality in pregnancy causing pancreatitis remains unknown. Liver-function tests and biopsies on pregnant women show no suggestive pattern in this regard (Ingerslev and Teilum, 1945; Day and Hellestrand, 1947; Dieckmann *et al.*, 1951). Boyd (1934) has shown that neutral fat, phospholipids, and cholesterol are all increased in the plasma during pregnancy, while Potter (1936) states that the gall-bladder is distended and that there is hypercholesterolaemia at term in most women.

The management of this disorder is poorly understood. Treatment has been conservative, surgery being indicated only in the presence of cholelithiasis, for the relief of obstructive jaundice, and for drainage of residual abscesses after an acute exacerbation. Internal biliary drainage by sphincterotomy does not seem to be indicated, because of the apparently normal state of the ducts and sphincters found in these patients, and the recent anatomical studies of Hughes and Kernutt (1954a) and of Sterling (1954).

Where symptoms of flatulence and pain have persisted the patient has been placed on a high-protein, low-fat diet and given atropine and ephedrine by mouth. It is not yet possible to speak of the efficacy of this regime or of the possible effects of further pregnancies in these patients. The recurrence of symptoms in Case 3 after cholecystectomy suggests that this syndrome may be one cause of the "post-cholecystectomy syndrome," although the normal biopsy finding in Case 4 two months after cessation of symptoms indicates that resolution may be complete.

Summary

Six cases are reported of young women who developed pancreatitis shortly after pregnancy. In all of them the clinical and laboratory findings were similar.

The aetiology of the pancreatitis is considered to be related to the preceding pregnancy, although the mechanism of this is unknown.

It is suggested that these patients, and others in the literature, form a distinct subgroup within the general group of patients with pancreatitis.

Until the aetiological factors are better understood, it is suggested that the term "post-partum pancreatitis" be applied to this subgroup.

My thanks are due to Dr. Ian Wood, head of the Clinical Research Unit, and Mr. E. S. R. Hughes for their interest and help in this work; to my colleagues in the clinical research unit for the many investigations performed on these patients; and to the physicians and surgeons who referred these cases. The photographs were prepared by Dr. J. D. Hicks and Mr. Roy Ingles, of the Royal Melbourne Hospital.

REFERENCES

Boyd, E. M. (1934). *J. clin. Invest.*, **13**, 347.
Burger, P. (1952). *Rev. franç. Gynec.*, **47**, 379. Abstract in *Int. Abstr. Surg.*, **97**, 372.
Cassel, W. J., jun., and Malewitz, E. C. (1950). *J. Amer. med. Ass.*, **142**, 1139.
Collett, R. W., and Kennedy, R. L. J. (1948). *Proc. Mayo Clin.*, **7**, 158.
Comfort, M. W., Gambill, E. E., and Baggenstoss, A. H. (1946). *Gastroenterology*, **6**, 239, 376.
—— and Steinberg, A. G. (1952). Ibid., **21**, 54.
Day, E. M., and Hellestrand, A. L. (1947). *Med. J. Aust.*, **2**, 326.
Deaver, J. B. (1918). *Ann. Surg.*, **68**, 281.
Dieckmann, W. J., Smitter, R. C., and Pottinger, R. E. (1951). *Surg. Gynec. Obstet.*, **92**, 598.
Dornberger, G. R., Comfort, M. W., Wollaeger, E. E., and Power, M. H. (1948). *Gastroenterology*, **11**, 701.
Fallis, L. S. (1951). *J. int. Coll. Surg.*, **16**, 337.
—— and Plain, G. (1939). *Surgery*, **5**, 358.
Gross, D. M. B. (1929). *J. Path. Bact.*, **32**, 503.
Haidlen, R. (1884). *Zbl. Gynäk.*, **8**, 609. Cited by Roberts *et al.* (1950).
Heffernon, E. W., and Gunter, A. R. (1951). *Gastroenterology*, **19**, 526.
Hicken, N. F., and McAllister, A. J. (1952). *Amer. J. Surg.*, **83**, 781.
Holt, L. E., jun., Aylward, F. X., and Timbres, H. G. (1939). *Bull. Johns Hopk. Hosp.*, **64**, 279.
Hughes, E. S. R., and Kernutt, R. H. (1954a). *Aust. N.Z. J. Surg.*, **23**, 223.
—— —— (1954b). *British Medical Journal*, **2**, 620.
Ingerslev, M., and Teilum, G. (1945). *Acta obstet. gynec. scand.*, **25**, 352. Cited by Dieckmann *et al.* (1951).
Joske, R. A., Saint, E. G., Hughes, E. S. R., and Bromilow, F. J. (1954). *Med. J. Aust.*, **2**, 473.
Kingsley, C. R. (1934). *N.Y. St. J. Med.*, **34**, 889.
Klatskin, G., and Gordon, M. (1952). *Amer. J. Med.*, **12**, 3.
Kunkel, H. G., Ahrens, E. H., and Eisenmenger, W. J. (1948). *Gastroenterology*, **11**, 499.
Langmade, C., and Edmondson, H. A. (1951). *Surg. Gynec. Obstet.*, **92**, 43.
Lawrence, W. (1831). *Med.-chir. Trans.*, **16**, 367. Cited by Langmade and Edmondson (1951).
Macnab, I. (1949). *British Medical Journal*, **1**, 568.
McWhorter, G. L. (1932). *Arch. Surg., Chicago*, **25**, 958.
Paxton, J. R., and Payne, J. H. (1948). *Surg. Gynec. Obstet.*, **86**, 69.
Potter, M. G. (1936). *J. Amer. med. Ass.*, **106**, 1070.
Roberts, N. J., Baggenstoss, A. H., and Comfort, M. W. (1950). *Amer. J. clin. Path.*, **20**, 742.
Rose, T. F. (1951). *Med. J. Aust.*, **2**, 453.
Saint, E. G., and Weiden, S. (1953). *British Medical Journal*, **2**, 1335.
Schmitt, W. J. (1818). *Sammlung zweifelhafter Schwanger-schaftsfaelle nebst einer kritischen Einleitung*, p. 172. Wien. Cited by Langmade and Edmondson (1951).
Sterling, J. A. (1954). *Surg. Gynec. Obstet.*, **98**, 420.
Warren, K. W. (1948). *Surg. clin. N. Amer.*, **28**, 741.
Watts, S. H. (1918). *Ann. Surg.*, **67**, 278.
Whipple, G. H. (1907). *Bull. Johns Hopk. Hosp.*, **18**, 391.
Wood, I. J., Doig, R. K., Motteram, R., and Hughes, A. (1949). *Lancet*, **1**, 18

TUBERCULOUS MESENTERIC ADENITIS IN CHILDREN*

BY

HUGH R. E. WALLIS, M.D., M.R.C.P., D.C.H.

Consultant Paediatrician, Bath Clinical Area; Medical Officer, Kingswood School, Bath

The purpose of this essay is to draw attention to a cause of minor illness in children which is usually overlooked in this country. It is intended to show that tuberculous mesenteric glands may sometimes cause symptoms and continue to do so even after they have become calcified.

The condition is well recognized on the Continent. Klein in 1927 reported cases from Poland and commented: "Beaucoup de médecins, en presence de cette maladie, ne croient pas à la possibilité de son existence." In Sweden, Strömbeck (1932) made a thorough review of the published work on the subject. Alexandre (1949), in France, gave another excellent account.

The symptoms described are colicky central abdominal pain, nausea, vomiting, sweating, meteorism, diarrhoea, constipation, pallor, lassitude, and loss of weight. The physical signs are palpable tumours in the abdomen, local tenderness, fever (especially in the evenings), and calcification visible in the *x*-ray film.

Most physicians, when confronted with calcified glands, assume that calcification signifies a healed lesion and that they must look elsewhere to account for the symptoms. If this assumption be true then we must assume also that the calcification appears suddenly and instantaneously, and that at that moment

*Condensed from the Nathaniel Bishop Harman Prize essay, 1954.

all symptoms cease. It would be better if we were to say, with the prisoner of Chillon (he was referring to his hair):

Nor grew it white
In a single night.

Strömbeck (1932) has shown the progress of calcification over a long period while symptoms continued, and in the cases here reported the same phenomenon has been demonstrated.

In this country the condition has received more attention from surgeons than from physicians (Carson, 1918; Struthers, 1921; Braithwaite, 1926). Rendle Short (1928) pointed out that an evening temperature rising to 100–101° F. (37.8–38.3° C.) may persist for months or even years.

More recently the condition appears to have been overlooked. This is probably because medical teaching centres are situated in large cities where the milk supplied to children is free from tubercle bacilli. Conway (1951) analysed the history and diagnoses of 250 children in London who complained of abdominal pain. Not one case of tuberculous mesenteric adenitis was discovered.

The following are some of the cases met with during a period of two years in consulting paediatric practice. They have been selected to show the different ways in which the disease may present itself. All the children were tuberculin-positive. All of them had had their chests *x*-rayed, and no tuberculous lesions were found. None of them had been in contact with infectious tuberculosis.

Case 1. Abdominal Pain

A boy who lived in the country and who had consumed raw milk from the age of 1½ years began to have attacks of pain in the left hypochondrium at the age of 8 years. This pain had no relation to meals, and occasionally woke him up. It was sharp and doubled him up, and was sometimes severe enough for him to be sent home from school. When it occurred he felt sick and turned pale. There were no abnormal physical signs. He was admitted to hospital with a tentative diagnosis of hiatus hernia or renal abnormality. His temperature, blood counts, urine, blood urea, *x*-ray films of the chest and sinuses, barium meal, and intravenous pyelogram were normal. An *x*-ray film of the abdomen showed calcified glands over the fourth and fifth lumbar vertebrae.

Progress.—He was treated with 20,000 units of calciferol daily for one month. A year later he had gained 4½ lb. (2 kg.) in weight. He still complained of pain occasionally, but it was not as severe as before. *X*-ray examination of his abdomen showed condensation of the calcium in the affected glands and a new area of calcification opposite the second lumbar vertebra.

Case 7. Incident Mimicking Acute Appendicitis

A Ukrainian girl who in early childhood had lived in Germany and had drunk raw milk there was admitted to hospital at the age of 11 as a case of acute appendicitis. She had then had intermittent pain in the right iliac fossa for six months. Her temperature was 100° F. (37.8° C.), pulse 92, and respirations 22. A blood count showed 8,200 white cells per c.mm. (72% polymorphs). Next day her temperature fell to normal and remained between 98 and 99° F. (36.7 and 37.2° C.) for five days. Her pulse rate remained below 100. Nevertheless on the seventh day her appendix was removed. The operation notes state that it was "inflammatory." She made an uninterrupted recovery.

Two and a half years later she was referred to the outpatient department complaining of abdominal pain in the left side. This was worse when she ran, but also occurred at rest. On examination there was some tenderness on deep pressure at the umbilicus. She was admitted for investigation, but no abnormality was found in the chest, heart, urinary system, or gastro-intestinal tract. *X*-ray examination of the abdomen showed some calcified glands in front of the fourth and fifth lumbar and the second and third sacral vertebrae.

Progress.—She was treated by a course of ultra-violet light and 20,000 units of calciferol twice daily for six weeks. Six months later she was well, and said that she had more energy. She had occasional pain, but it occurred less often. The glands were palpable just below the umbilicus. *X*-ray examination showed an increase in the calcification of those in the pelvis, whilst the others were unchanged. Three months after this she had no pain at all.

Case 5. Abdominal Pain and Vomiting. Primary Infection Observed

A girl who lived in the country and had raw milk began to complain at the age of 4 of left-sided abdominal pain at intervals. She was usually constipated, and occasionally had frequency of micturition and pain on passing water. In one of these attacks she vomited once and was admitted to hospital in another part of the country. The summary of her notes states: "On examination, a rather pale unwell-looking child. E.N.T. normal. Chest clear. Abdomen slightly resistant to palpation, especially in the left renal angle. Physical examination otherwise showed no abnormalities. Progress and investigations: urine × 6 normal; Hb 89%; W.B.C. 10,000; Mantoux 1 in 1,000 positive; *x*-ray film of chest, no lesion seen; E.S.R. 10 mm. in one hour. She was allowed up before discharge, during which time she appeared well and made no complaints. Discharge note: the period of ill-health during the last 18 months was possibly due to a primary tuberculous complex. There is no evidence of activity now."

During the next two and a half years she had repeated attacks of abdominal pain lasting for periods varying up to a week. In one attack she began to vomit, and her general practitioner referred her to hospital with the following note of his findings and opinion.

"Pale and looks ill. Temperature 100.5° F. (38° C.), pulse 90. There is a tender knobbly mass in the left iliac fossa. Per rectum, *very* tender anteriorly. I feel sure the diagnosis is tuberculous adenitis, but I cannot exclude a low-grade appendix or other pathology." The patient was admitted and the findings were confirmed. Investigations showed a normal blood count. E.S.R. 15 mm. in one hour (Westergren). Several examinations of urine for tubercle bacilli were negative. *X*-ray film of the abdomen showed several large calcified glands to the left of the fourth and fifth lumbar vertebrae and one small gland to the right of the third lumbar vertebra. An intravenous pyelogram showed no abnormality, and the calcified opacities were seen to be separate from the renal tract.

Progress.—The patient was treated with 20,000 units of calciferol twice daily for one month and a course of ultra-violet light. Her temperature subsided rapidly. Five weeks later she had gained 9 lb. 12 oz. (4.4 kg.) and had less pain. A year later she was very well, had gained 16 lb. (7.3 kg.) since admission, and had no pains or sickness.

Case 17. Pyrexia of Unknown Origin. Tuberculous Rheumatism

A boy who lived in the country and had drunk raw milk regularly complained of pain in the left knee and groin at the age of 7½ years. He was admitted to hospital with a diagnosis of synovitis of the left hip. This was considered to be a simple synovitis, not tuberculous, and he was transferred to an orthopaedic hospital. His temperature was normal. The E.S.R. was 2 mm. in one hour (Westergren). A blood count and his urine were normal. A chest *x*-ray film was normal. The condition was treated by simple traction, and six weeks later it had improved considerably. The boy's temperature, however, was raised to 99.4° F.

(37.4° C.), or even 100° F. (37.8° C.) in the evenings, and the orthopaedic surgeon in charge could not explain this. The E.S.R. had risen to 38 mm., and his weight was stationary. A second *x*-ray film of the chest was normal. The urine contained no pus cells or tubercle bacilli. *X*-ray examination of the abdomen showed calcified glands on the right side of the fourth lumbar vertebra. It was considered that the cause of the temperature was the mesenteric adenitis, and that the synovitis of the hip was a manifestation of tuberculous rheumatism.

Progress.—He was treated by rest in bed, ultra-violet light, and 20,000 units of calciferol daily for a month. At the end of this time his temperature had settled, his E.S.R. was 11 mm. and he was discharged home. Two months later he had gained 4 lb. (1.8 kg.) and was very well. His mother stated that he had an enormous appetite. A year later he was very well and had no symptoms. *X*-ray examination showed no change in the glands.

Case 19. Coeliac Syndrome

This boy, who lived in the country and drank raw milk, suffered from phlyctenular conjunctivitis at the age of 2 years. Two years later he complained of anorexia and vomiting, and upper abdominal pain. His abdomen appeared to be "blown out with wind." His stools were loose and offensive. He was admitted to hospital, where his weight was found to be 30 lb. (13.6 kg.). The stools were typical of the coeliac syndrome. A fat-balance test showed only 66% absorption of fat. Trypsin was present in several specimens of stool. One physician who saw him commented, "On clinical grounds I do not think that this can possibly be coeliac disease because he is so happy and cheerful, and there has never at any time been any wasting of his muscles." He suffered from a microcytic type of anaemia. *X*-ray examination of the abdomen showed calcified glands to the left of the second lumbar vertebra.

Progress.—He was given iron for the anaemia, but had no special treatment for the coeliac syndrome. He did very well, and when seen 13 months later had gained 6 lb. (2.7 kg.) and grown 2 in. (5 cm.). He had no pain or diarrhoea. *X*-ray examination showed the glands to be more firmly calcified.

Summary of Cases

Altogether 20 children were seen in whom tuberculous mesenteric glands were considered to be causing symptoms. Of these, 14 had pain as the main complaint, one had pain and pyrexia, four pyrexia alone, one showed the coeliac syndrome, and one was a case of primary infection. Details of these cases are given in the Table. There were 15 boys and five girls.

Details of Cases

Case No.	Sex	Age at Onset (Years)	Length of History	Nature of Case	Site of Glands (Quadrant of Abdomen)
1	M	8	4 weeks	Abdominal pain	Left upper, central
2	M	5	1 year	,, ,,	Right lower
3	M	9	4 months	,, ,,	Left upper, right lower
4	M	7	3 ,,	Abdominal pain, tuberculous rheumatism	Left lower
5	F	4	2½ years	Abdominal pain	,, ,,
6	F	6	2½ ,,	,, ,,	Right ,,
7	F	13	6 months	,, ,,	Central, pelvic
8	M	9	1 month	,, ,,	Right lower
9	F	8	2 years	,, ,,	Pelvic
10	M	3	3½ ,,	,, ,,	,,
11	M	6	1 year	,, ,,	Right lower
12	M	3	9 months	,, ,,	,, ,,
13	M	2	7 years	,, ,,	,, ,,
14	M	5	7 months	,, ,,	Left ,,
15	M	10	1 week	Abdominal pain, pyrexia	Right ,,
16	M	6	1 month	Pyrexia	Pelvic
17	M	7	Found in hospital	Pyrexia, tuberculous rheumatism	Right lower
18	F	9	,,	Pyrexia	Left ,,
19	M	4	8 months	Coeliac syndrome	,, upper
20	M	2	Nil	Primary infection	,, ,,

The age of onset was fairly evenly spaced throughout the third to eleventh years of life. The duration of symptoms before the first contact with a paediatrician varied from one week to seven years. Most cases were seen during the first year, and a small group at two to four years. The average length of history was one year four months.

All the patients except one lived in the country. The exception was a boy living in Bath who had previously lived in the country.

The glands demonstrated by *x*-ray examination were most often seen in the area of the ileo-caecal junction, but there were nearly as many along the line of attachment of the mesentery of the small intestine. In four cases the glands appeared to be in the pelvis. In two cases in which the infection took place at an early age the glands were demonstrated high up to the left (Cases 19 and 20). It may be that early or overwhelming infection occurs high up in the small intestine in an area which drains into glands on the left of the midline, whereas later and milder infections take place lower down the gut, where the mesentery is attached to the right side of the abdomen. In the infants at Lübeck the majority of the glands were found on the left.

In four of the cases it was possible, on looking back, to disclose illnesses which might have been due to primary infection (Cases 4, 5, 6, and 7). In one case the primary infection was observed in hospital and the glands were discovered by chance when the patient returned later with a different illness (Case 20).

Differential Diagnosis

The condition must be differentiated from non-tuberculous causes of pain, pyrexia, or vomiting, and these are legion. During the two-year investigation described below the following diagnoses were made in children who complained of abdominal pain; acute nephritis, dietary indiscretion, empyema, hernia of the linea alba, idiopathic epilepsy, idiopathic thrombocytopenic purpura, inadequate dentition, non-specific mesenteric adenitis, pneumonia, psychological disturbance, pyelitis, recurrent neutropenia, and salmonella food-poisoning. The causes of pyrexia are too numerous to mention.

If the tuberculin test is positive it is important to make sure that there is no active tuberculous lesion in any other organ. Pulmonary tuberculosis, especially when accompanied by pleurisy, may cause abdominal pain; and tuberculous peritonitis and inflammation of the spine must also be considered. Affection of the renal tract must be excluded by repeated examination of complete morning specimens of urine for pus cells and tubercle bacilli.

The radiological appearance of tuberculous glands is usually unmistakable. They are round or oval; the shadows are not homogeneous, but mottled, and appear like a mulberry or an archipelago as seen on a map. They may lie anywhere in the abdomen, but are usually seen along the line of attachment of the mesentery of the small intestine. In the lateral view they are often in front of the spine.

During the two-year survey other causes of shadows in the abdomen found were: stones in the gall-bladder, calcified phleboliths in a girl with multiple angiomata, calcification in an adrenal neuroblastoma, and various pills and tablets. No renal stones were seen.

The Lübeck Catastrophe

At Lübeck in 1930 virulent tubercle bacilli were administered inadvertently by mouth to 251 infants (Schürmann and Kleinschmidt (1935). Seventy-two died from tuberculosis within a year. Practically all the children who developed primary lung lesions died, while the majority who had primary alimentary lesions survived. In many cases the abdominal infection produced no symptoms or very vague ones. Calcification of the abdominal glands was seen at the earliest 18 months after the infection; and after

three years it had reached its final stage. Late results such as obstruction and the coeliac syndrome were not observed.

X-ray films were taken of 173 children at 4 years of age, and 126 of them had calcification in the abdominal glands. This was rather more common on the left side, suggesting that the site of infection was usually high up in the small intestine.

One most important point is the benign course of the disease in the abdomen compared with the serious outcome when the lungs were affected.

Treatment

In the majority of cases the disease proceeds to heal spontaneously, and it may be that there is no need to interfere with this natural process. Previous workers have usually approached the problem from the surgical angle. Arguments have been put forward for and against removal of the affected glands. It has been pointed out that sometimes when the diagnosis is in doubt it is imperative to operate rather than run the risk of neglecting to remove an acutely inflamed appendix. It has also been noted that after an exploratory laparotomy tuberculous mesenteric adenitis may improve in a spectacular manner, even though the glands are not removed, just as tuberculous peritonitis may.

Wallace (1946) and Gauvain (1948) have reported favourably on the calciferol treatment of tuberculous glands in the neck. Macrae (1947) has studied the effect in tuberculous peritonitis. Gauvain stated: "Calciferol causes an early flare-up of activity, followed generally by rapid healing, which is of such a sound degree that the glands can be immediately and, so far as we can tell at this early stage, safely excised with little risk of recurrence."

The dose of calciferol used by Gauvain was 100,000 units daily for several months. Macrae used even larger doses. He reported some alarming reactions. One of his patients died from haemoptysis from a very small cavity, the presence of which had been unsuspected. None of the patients consuming large doses of vitamin D felt fit, and all of them lost weight.

Results of Treatment.—It seemed that it might be dangerous to produce a flare-up in the abdominal glands, and that the ideal to aim at would be to produce a more gradual healing, imitating the natural process, but gently expediting it. It was therefore decided to give the children only 40,000 units of calciferol daily and to support this with a course of ultra-violet irradiation when this could be conveniently arranged. The treatment was continued for six weeks. Results are difficult to assess in a condition which usually proceeds to spontaneous cure. The numbers available are not sufficient for definite conclusions to be drawn, but on the whole the impression was that treatment gave considerable benefit. In most children the pains abated, the appetite improved, the weight increased, and after three to six months there were no more symptoms.

Flare-up.—Two of the treated children (Cases 8 and 16) demonstrated phenomena which might be considered to be due to mild exacerbations or flaring up of the disease. Neither was seriously inconvenienced and both were eventually regarded as cured.

Case 16.—A boy aged 6 years who lived in the country and consumed raw milk complained of pain in the legs and had fever of 99 to 100° F. (37.2 to 37.8° C.) for a month. He was admitted to hospital and found to have a positive tuberculin reaction. Calcified glands in the presacral region were seen on the *x*-ray film. Other investigations were negative. He was treated with calciferol and ultra-violet irradiation. Two months later he stated that he had had two attacks of abdominal pain lasting for two days. The pain was colicky and was felt at the umbilicus. He had lost 1½ lb. (0.7 kg.) in weight in the first month, but had regained it. Three months after this he had had no pain or pyrexia. He had gained over 5 lb. (2.3 kg.). *X*-ray examination showed firmer calcification.

Recommendations

When active tuberculous mesenteric adenitis has been diagnosed as the cause of symptoms it seems reasonable to recommend that the child should be given the benefit of treatment with calciferol. A convenient dose is 50,000 units daily, as tablets are made in this strength. This treatment is not expensive: the retail price of 50 tablets is 2s. 9d. and 500 cost 19s. 6d. Treatment should be continued for six weeks. In this dosage no fear need be entertained about toxic symptoms, but if headache, anorexia, or vomiting occurs the situation should be reviewed, especially with regard to raised blood pressure and protein in the urine.

In the acute case in which the possibility of appendicitis has to be considered a count of the white blood cells may be of value. If this is low or normal and an *x*-ray film of the abdomen shows calcified glands a policy of watching in hospital is probably justified. If there is any serious doubt it is better to proceed with a laparotomy.

There is no justification for treating this mild disease with streptomycin, para-aminosalicylic acid, or isoniazid.

Incidence in Consulting Practice

The Bath clinical area consists of a city of some 90,000 inhabitants and a large surrounding rural region with a total population of approximately 200,000. For medical purposes the area is covered by two consultant paediatricians. An analysis was made of all patients seen by one of these paediatricians during a period of two years (from October 1, 1951, to September 30, 1953, inclusive).

The total number of children seen for the first time either in the out-patient department or in the wards was 825. In 58 (7.03%) of these the main complaint was abdominal pain. Eight of the 58 had pyrexia also. Twenty-two other children were referred for pyrexia alone (2.73%).

Of the 58 children with pain 8 had tuberculous abdominal glands (13.79%). Of the 22 with pyrexia 1 (4.55%) had infected glands. Of the 80 who had either pain or pyrexia nine had infected glands (11.25%).

Relation to the Tuberculin Test.—Of the 58 cases with pain, 13 were tuberculin-positive. Eight of these had active tuberculous glands. Of the other five, one had a tuberculous infection of the lung, one a hernia of the linea alba, and in the remaining three cases a diagnosis could not be made. It may be that some of these children were undergoing a tuberculous process in the abdomen in which calcification had not yet appeared, or would never appear. Follow-up has so far revealed no such calcification.

Comparison With Tuberculosis of Other Systems.—During the two-year period, in addition to the nine cases of tuberculous mesenteric adenitis, one case of tuberculous peritonitis was encountered. There were 10 cases of tuberculosis of the lungs, two cases of tuberculous meningitis (both with primary lesions in the lung), one case of phlyctenular conjunctivitis, and one of tuberculous cervical adenitis. The total number of cases of active tuberculosis was 24. In 10 of them the abdomen was principally affected, and in 14 it was not. It may be inferred that in this clinical area abdominal tuberculosis is very nearly as important as the pulmonary variety.

In passing, three children were found to have healed calcified lesions in the lung, and two had healed inactive glands in the abdomen.

Incidence in a Group of Schoolboys

This is not a satisfactory control series. It is made up of boys only, of a social status not comparable to that of the population at risk. However, it consists of observations on healthy normal children who were not selected by reason of any medical symptom, and the results obtained were so startling as to be worthy of publication.

The boys were boarders aged 11 to 16 entering a public school in two successive years. They came from all parts of the country. A large number of them were the sons

of parsons; the rest were mainly sons of other professional men. Of the 128 boys seen and tested with tuberculin jelly, 25 reacted positively. These 25 boys were subjected to *x*-ray examination, and 18 (72%) of them were found to have calcified abdominal glands. One had calcified glands in the neck as well. Four (16%) had healed lesions in the lung, and the remaining three (12%) had no demonstrable tuberculous lesion.

The parents of the 18 boys with abdominal glands were asked for details of any unexplained pain, pyrexia, or obscure prolonged illness in the past. Seven reported unexplained pain and pyrexia, one pain and vomiting, one pain and anorexia, and one pyrexia alone. Only eight could recollect no symptoms at all. That the illnesses were not minor is shown by the following extracts (verbatim) from the replies.

Case 21.—"From the age of 4 years his health history has been one of recurring attacks of headache, raised temperatures, vague tummy-aches, intermittent diarrhoea, and marked lethargy. . . . He saw a number of doctors in each place where we lived, but none could find a reason for the symptoms, and I was assured 'He would probably grow out of it.' He was *x*-rayed in —— about two years ago; three doctors failed to agree on the diagnosis. The tuberculosis specialist said there was nothing 'in his department'; but our doctor was not so happy about it, and, acting on his advice, I put the boy to bed for six months' complete rest. Since then he has seemed better."

Case 22.—"When he was 2 years old he first complained of a pain in his abdomen, but it did not trouble him very much. When he was 2½ he suddenly ran a temperature. We called in a doctor, who seemed unable to diagnose. When he was almost 5 he again ran a temperature, and very shortly afterwards our doctor suggested we called in a specialist. He examined him thoroughly, but could find nothing abnormal. After a further slight recurrence at about 7 years I arranged for Professor —— to examine him, and he too could not find anything wrong. Since then he has had occasional spasms of pain which were relieved by resting for a short while."

Case 24.—"He certainly has had stomach pains, in which case we have always called our doctor in, but he has never been able to find anything wrong with him. Incidentally, he has for a period of a week run abnormally high temperatures, for no apparent reason, not once but many times. Secondly, he was always complaining of feeling very tired. I used to think he was lazy, when the doctor assured me at all times that he was a very healthy boy."

Case 26 (son of a medical man).—"He had repeated attacks of tonsillitis, and occasional attacks of abdominal pain when he was younger. I made the diagnosis at that time of tuberculous ileo-caecal glands, and *x*-ray examination of the abdomen at the age of 8 revealed what you have found—a calcified mass in the right iliac fossa."

Case 28 (from the family doctor).—"Six years ago he had symptoms of appendicitis, and a laparotomy was done. The appendix was mildly inflamed and there were definite tuberculous glands in the right iliac fossa."

Milk Supply

Abdominal tuberculosis is usually thought to be contracted by drinking infected milk. There are occasions when it may be traced to contact with open cases of pulmonary tuberculosis, but they are rare. Toddlers put most small objects in their mouths, and may thereby ingest some dried sputum from dust on the floor or road. Ashby (1923) reported cases of abdominal tuberculosis from Manchester in which no unboiled milk had been drunk. Strömbeck (1932) refers to cases occurring in Japan in 1904, when cow's milk was unknown as a food there.

Pasteurized and tuberculin-tested milks are usually considered to be safe. Pasteurized milk has been proved to be satisfactory and a stringent check is kept on its production. Tuberculin-tested milk, however, may occasionally contain tubercle bacilli. The intervals between inspections are fairly long and tuberculous cows are occasionally found in the herds. The danger arising from this is made worse by the practice of bulking milk in 1,000-gallon (4,500-litre) containers for transport. Accredited and non-designated milks cannot be regarded as free from infection.

In the cases described above it was usual to obtain a history of drinking raw milk for prolonged periods, though the parents of some of the children would admit to no such exposure.

Wilson *et al.* (1952), writing on infection with bovine tubercle bacilli, state: "Many of the records suggested that the consumption of raw milk must have been only slight or occasional, pointing to the danger of drinking raw milk at any time or in any form."

It is possible that one draught of raw milk is enough to start a primary infection; and there must be few country children who have not at some time had a glass. However careful their parents may be, children are bound to go out for meals or snacks sometimes and to drink milk of unknown quality. Perhaps boys will do so more than girls, and this may be the explanation of the preponderance of boys in the series.

Of the milk supplied by retailers in Bath in 1953 85% was heat-treated, 14% tuberculin-tested, and only 1% raw. In Wiltshire, however, in the same year, 12.16% was heat-treated, 50.72% tuberculin-tested, and 37.12% raw. Some of the raw milk was transported out of the county and pasteurized elsewhere (mainly in London), but the situation is nevertheless alarming.

Figures for morbidity and mortality of non-pulmonary tuberculosis show the result of this. The morbidity rate for non-pulmonary tuberculosis in Wiltshire in 1952 was 0.1673 per thousand, compared with 0.1200 for Bath and 0.1410 for England and Wales. The death rates for 1952 were: Wiltshire, 0.0309, Bath, 0.0000, England and Wales 0.0280.

It would be fair to comment that a number of deaths occurred in the county from a disease which could and should be prevented. At some future date the county will become a "designated area" under the Milk (Special Designations) (Specified Areas) Order, 1952, and from then on the condition described in this essay will gradually become rarer until it goes the way of scurvy, rickets, and congenital syphilis.

Summary

Attention is drawn to the importance of tuberculous abdominal glands as a cause of pyrexia and abdominal pain in childhood. Twenty cases are described, including examples presenting with pain, pyrexia, attacks resembling acute appendicitis, tuberculous rheumatism, and the coeliac syndrome. Reference is made to the experience at Lübeck in 1930.

Treatment with 50,000 units of calciferol daily for six weeks is recommended as a means of expediting the natural process of healing. This is not expensive.

The incidence of abdominal tuberculosis has been investigated. It is concluded that in the area under review it is now nearly as common as pulmonary tuberculosis. It seems to be more common in boys than in girls.

A survey of unselected normal schoolboys led to the discovery of further cases which had in the past caused baffling symptoms. In this group abdominal tuberculosis was more common than pulmonary.

The relation between the incidence of the disease and the consumption of raw milk is discussed.

I have much pleasure in placing on record my thanks to Dr. John Apley for his continued encouragement and for providing ready access to cases under his care; and to the consultant

surgeons of the Bath clinical area, particularly Mr. F. Kohn, who assisted with the translation of the account of the Lübeck disaster; the general practitioners who referred cases: Drs. O. H. Blacklay, D. Hall Brooks, C. J. C. Davey, M. Dietrich, J. D. O. Fearnley, R. J. K. Fleming, B. Hancock, B. L. Hodge, A. K. James, A. E. K. Price, W. H. Royal, J. A. Taylor, C. N. Vaisey, and W. Winch; Dr. B. A. Astley-Weston, M.O.H. for Bath; Dr. J. Burman Lowe, lately M.O.H. for Wiltshire; Dr. C. D. L. Lycett, M.O.H. for Wiltshire; Dr. J. F. Davidson, M.O.H. for Somerset; Dr. P. Mann for advice on epidemiological matters; my house-physicians; Miss R. Tilden-Smith (sister in charge of the sanatorium at Kingswood School); Dr. S. Gauvain for information; the consultant radiologists, Drs. H. J. Johnson, G. D. Steven, and A. C. P. D. Thomson, for their ready co-operation; and Dr. Victoria Smallpeice for information about Case 5.

ADDENDUM.—Since this essay was written cases of tuberculous mesenteric adenitis have been encountered with undiminished frequency, and another case of tuberculous rheumatism has been seen. The main problem encountered has been the diagnosis of cases in which the clinical picture is typical, the tuberculin test is positive, no other tuberculous lesion can be found, but no calcification is seen on *x*-ray examination. In these cases the diagnosis is vague, being arrived at by exclusion and therapeutic test. The use of radioactive calcium for tracing the process of calcification in the glands might be of value. Unfortunately no suitable isotope has yet been discovered.

REFERENCES

Alexandre, P. (1949). *Sem. Hôp. Paris*, **25**, 3862
Ashby, H. T. (1923). *British Medical Journal*, **2**, 863.
Braithwaite, L. R. (1926). *Brit. J. Surg.*, **13**, 439.
Carson, H. W. (1918). *Trans. med. Soc. Lond.*, **41**, 220.
Conway, D. J. (1951). *Gt Ormond St J.*, **1**, 99.
Gauvain, S. (1948). *Tubercle (Lond.)*, **29**, 259.
Klein, S. (1927). *Rev. Tuberc. (Paris)*, **8**, 340.
Macrae, D. E. (1947). *Lancet*, **1**, 135.
Schürmann, P., and Kleinschmidt, H. (1935). *Arb. ReichsgesundhAmtes.* **69**, 1.
Short, A. Rendle (1928). *Lancet*, **2**, 909.
Strömbeck, J. P. (1932). *Acta chir. scand.*, **70**, Suppl. 20.
Struthers, J. W. (1921). *Edinb. med. J.*, **27**, 22.
Wallace, H. J. (1946). *Lancet*, **2**, 88.
Wilson, G. S., Blacklock, J. W. S., and Reilly, L. V. (1952). *Non-pulmonary Tuberculosis of Bovine Origin in Great Britain and Northern Ireland.* N.A.P.T., London.

A COMPARISON OF VACCINATION WITH VOLE BACILLUS AND B.C.G. VACCINES

BY

HUGH W. O. FREW, M.D., D.P.H.
Area Supervising Tuberculosis Physician, Renfrewshire and Bute Chest Department

J. ROMANES DAVIDSON, M.D.
Medical Superintendent, Orphan Homes of Scotland

AND

J. T. W. REID, M.B., Ch.B., D.P.H.
Deputy County Medical Officer, County of Renfrew

B.C.G. vaccine was first used as a measure to prevent tuberculosis in human subjects in 1922. While, so far, there is no direct evidence that B.C.G. vaccination does in fact protect against tuberculosis, the experience gained in many countries, such as Denmark, goes far to support such a contention, and the vast majority of tuberculosis physicians throughout the world advocate the extension of anti-tuberculosis vaccination, believing that if it was adopted on a wide scale it would quickly reduce the number of new cases. A murine form of acid-fast bacillus found in voles was described in 1937 by Wells (1946), and from this organism he prepared a vaccine which he showed produced tuberculin conversions and acted in a manner very similar to B.C.G.

The course of vaccination with B.C.G. has been fully described; it is usually uneventful and produces little or no discomfort. However, there appear to be good reasons for carrying out investigations into new forms of vaccination. B.C.G. vaccine is not necessarily the ideal immunizing agent, as it is an artificial organism which might lose its potency. It would be wise to have available a proved substitute, and vole vaccine might well be suitable.

Any investigation of the action of vole vaccine must be controlled by a corresponding group treated with B.C.G., and all the conditions regarding surroundings and observations must be identical.

As vaccination with either B.C.G. or vole vaccine is a harmless procedure, neither giving rise to any systemic reactions, a comparison between the two vaccines can best be made by noting the ease of administration; the conversion rates; the early local reactions; the reversion rates; and the late reactions, or the late cosmetic effects. The final comparison must obviously include a note of any subjects who subsequently develop tuberculous disease. This is a matter of a long-term observation and cannot be completed until a period of at least fifteen to twenty years has elapsed.

The present investigation, which is being carried out at the Orphan Homes of Scotland, Bridge of Weir, began in the autumn of 1951. Of the 783 children between 1 and 15 years of age resident in the homes, the 575 included in the initial series and the 130 in subsequent series were negative reactors to 100 I.T.U., using old tuberculin. Details of the preliminary tuberculin survey have already been reported (Frew *et al.*, 1953). In all the cases *x*-ray examination by the M.M.R. unit failed to show any chest lesions. For the principal series, in 1951, two equal groups were selected by random methods, care being taken to ensure that both groups were as nearly as possible equal in regard to sex, age, school class, and cottage. B.C.G. was given to 288 children and vole vaccine to 280.

Administration

The B.C.G. vaccine was obtained from normal supplies prepared in the State Serum Institute in Copenhagen and given in the normal manner.

The vole vaccine used was in three forms: (*a*) Dry, reconstituted vaccine (2 mg. dry weight per ml.), used in 1951. (*b*) Liquid vaccine (2 mg. dry weight per ml.), used in 1952. (*c*) Liquid vaccine (half-strength) (1 mg. dry weight per ml.), used in 1953.

In 1951 the under-5-year group (numbering 55) were given the vole vaccine by intradermal injection, the dosage and method being identical to those used for B.C.G. In the case of the children of 5 years and over, vaccination was carried out by multiple puncture. The apparatus used consists of a spring-loaded gun which, on release of the trigger, projects 40 needles through a predetermined distance. For the present work the needles were adjusted to penetrate a depth of 2 mm. A sterile circle of rice paper of the same diameter as the end plate of the gun was dipped into the vaccine, applied smoothly to the skin, and the punctures were made through it. Little pain was felt, many of the children stating that they felt only a dull knock, and no dressings were required.

Conversion Rates

1951 Group.—Routine tuberculin-testing was begun at the end of the second week and was continued at weekly intervals until each case was recorded as positive. In children of 5 years and over, Mantoux-testing, using 100 units old tuberculin, was used, while in children under 5

years the tuberculin jelly test was used without flourpaper. The conversion rates for the various groups are shown in Table I. Very rapid conversions were noted in the B.C.G. group, the percentage after three weeks being 93% (99% in those over 5 years of age). The conversion rate in the vole group was slower, being 66% after three weeks and 79% after four weeks. Table I shows, however, that by

TABLE I.—*B.C.G./Vole Conversion Rates*

	Total	Positive				
		2nd Week	3rd Week	4th Week	6th Week	8th Week
		B.C.G.				
Kindergarten (1–4 yrs.)	56	18 (32%)	39 (70%)	48 (86%)	53 (95%)	55 (98%)
Primary Sec. and outside schools	174	86 (49%)	171 (98%)	172 (99%)	173 (99%)	174 (100%)
	58	48 (82%)	58 (100%)	58 (100%)	58 (100%)	58 (100%)
	288	152 (53%)	268 (93%)	278 (96·5%)	284 (98·6%)	287 (99·6%)
		Vole				
Kindergarten (1–4 yrs.)	55	18 (32%)	42 (76%)	53 (96%)	54 (98%)	55 (100%)
Primary Sec. and outside schools	169	27 (16%)	102 (60%)	119 (70%)	160 (94%)	167 (98·8%)
	56	27 (48%)	40 (71%)	49 (87%)	53 (95%)	56 (100%)
	280	72 (26%)	184 (66%)	221 (79%)	267 (95%)	278 (99·3%)

the sixth week the percentages were B.C.G. 98.6% and vole 95%; and 99.6% and 99.3% at the eighth week. Further testing at 12 weeks showed that in both groups there was a final 100% conversion. It was also noted that in the under-5-year group (intradermal vole) the rate of conversion was more rapid than in the corresponding B.C.G. group, and it is interesting to note that subsequent tuberculin testings at 6, 12, and 24 months have shown that no reversions have occurred in this vole group.

1952 and 1953 Groups.—In these groups tuberculin-testing was carried out at three and six weeks, and by the latter date complete conversion had taken place (Table II).

TABLE II.—*Vole Vaccine Conversion Rates*

	Total	3rd Week	6th Week
1952	38	−5 years 42% +5 „ 92%	100%
1953	49	−5 „ 38% +5 „ 86%	100%

Local Reactions: 1951 Series

B.C.G.—The reactions followed the usual course—macule, papule, and ulcer. On the whole they were rather more severe than expected and greater than met with in similar groups vaccinated as contacts or school-leavers. In the under-5-year group ulceration was noted in 96% and enlargement of the axillary glands in 48%. This adenitis was first noticed at five weeks, but in two cases it did not develop until the fourteenth week. In only one case did the condition progress to abscess formation. The average diameter of the ulcers noted was 4–5 mm. They were usually at their largest at approximately seven weeks, and healing occurred in from eleven to twenty weeks. In the children of 5 years and over ulceration was noted in the majority. The ulcers were on an average from 5 to 8 mm. in diameter (in nine it exceeded 8 mm.); they were at their greatest size at from five to eight weeks and healing took place in a very variable time from nine to twenty-six weeks. In five cases an axillary abscess formed between the third and ninth months, and in two cases acid-fast bacilli were demonstrated in the pus obtained from the abscesses. The presence of pus did not seem to have any adverse effect on the rate of healing or on the rate of conversion. Auto-inoculation was noted in a number of cases—usually on the skin of the arm adjacent to the vaccination.

Intradermal Vole.—The local reactions in this group were marked by their severity. Deep ulcers were noted in 100% of the cases, and all showed enlargement of the axillary glands. This adenitis was first noted at three weeks, and in all cases was present by eight weeks. Axillary abscesses occurred in 25 cases, or 45%. Several of these axillary abscesses were late in developing. Examination of the pus obtained from these glands showed acid-fast bacilli in 18 out of the 25 cases. The ulcers were 7 to 8 mm. in diameter, were deep, and reached their largest at seven to eight weeks, and, on an average, healing took place in from fourteen to twenty-eight weeks. A feature of this group was the very satisfactory healing which followed the admittedly very severe local reactions.

Multiple Puncture Vole.—In vaccination by multiple puncture no generalized reactions were noted and no child complained of pain or discomfort. The typical rosette began to develop in two to three weeks and varied greatly in size. Ulceration was noted in one case, but this was due to secondary infection following a severe blow on the vaccination site. In only three cases did an abscess develop in the axillary glands—one at a very late date—and in none of these cases was this complication accompanied by any systemic upset. Acid-fast bacilli were demonstrated in the pus obtained from the glands in all three cases. In no case was there any suggestion of auto-inoculation.

Local Reaction: 1952 and 1953 Series

The multiple-puncture vole vaccinations followed the pattern already described. The development of the rosettes was more satisfactory and the percentage of complete rosettes greater than in 1951. A 100% conversion was obtained by the sixth week.

Reversion Rates: 1951 Series

The data so far collected, relating to reversions, concerns the 1951 series only. Tuberculin-testing was carried out at six months, one year, and two years. As before, Mantoux-testing was employed in those aged 5 years and over, and the tuberculin jelly tests—without using flourpaper—in the under-5-year group. The initial Mantoux tests were carried out using 10 I.T.U. and all negative reactors were retested with 100 I.T.U.

Since the beginning of the investigation an increasing number of children have left the homes. We have made every effort to have these children followed up by the local public health departments, but unfortunately it has not been possible to carry out the periodic tuberculin-testing in all. The number of reversions reported here are a percentage of the children actually tested at the periodic surveys.

Table III shows that the percentage of reversions at six months and one year showed little difference between B.C.G. and vole groups, but by the end of the second year the

TABLE III.—*Reversion Rates*

	Under 5 Years				5 Years and Over			
	Vole		B.C.G.		Vole		B.C.G.	
	No. Tested	Reversions	No. Tested	Reversions	No. Tested	Reversions	No. Tested	Reversions
Start ..	55		56		225		232	
6 months	54	0	55	0	223	0	219	2 (0·9%)
1 year	53	0	54	1	221	4 (1·8%)	217	4 (1·8%)
2 years	50	0	45	1	200	14 (7%)	195	20 (10·3%)

percentage of reversions was higher in the B.C.G. group. Furthermore, no reversions had occurred in the intradermal vole group at the end of the second year. No case which had reverted to negative at one year was found to be tuberculin-positive at two years. It was noted at each routine tuberculin-testing that a number of cases required retesting with 100 I.T.U. The number of such cases was small at six months, larger at one year, and much greater at two

years. The number of children requiring retesting was definitely greater in the B.C.G. than in the vole group (Table IV).

TABLE IV.—*Cases Requiring Retesting with 100 I.T.U.*

	Vole					B.C.G.				
	No. Tested	−5	5+	Total	%	No. Tested	−5	5+	Total	%
6 months	277	—	12	12	4	274	1	19	20	7·3
1 year ..	274	3	37	40	14·6	271	1	71	72	26·6
2 years..	250	4	61	65	26	240	10	86	96	40

It is too early to place much importance on these figures, but they appear to suggest a greater diminution of allergy in the B.C.G. than in the vole group.

The percentage of reversions would seem to be high. Routine retesting of a group of contacts in the County of Renfrew shows a reversion rate of 1.5% after two years and 5.2% after three years. In this connexion it should be noted that the children in the homes were all examined by the M.M.R. unit each year and that no cases of active tuberculosis were found at any of these visits. They therefore did not receive the minimal doses of infection such as one would expect if they had been living outside the homes, and this fact is very possibly responsible, at least to some extent, for the high reversion rate.

Reversion Rates: 1952 Series

Routine tuberculin-testing carried out at one year confirmed these findings. The fact that further tuberculin-testing with 100 I.T.U. was required in 26.5% of the B.C.G. group as against only 5.1% of the vole group again suggests that the allergy produced by the vole vaccine is more permanent, or at least stronger, than that resulting from vaccination with B.C.G.

Late Cosmetic Results: 1951 Series

The late results of the B.C.G. vaccinations were those normally observed, and no ugly or objectionable scarring was noted. It was particularly pleasing to note the excellent healing and absence of bad scars which followed intradermal vole vaccination in spite of the severe early reactions. In multiple-puncture vole vaccinations the routine weekly inspections showed that the individual puncture marks developed induration which became progressive and subsequently increased over a period of nearly one year. This induration was first noted in the older children during the seventh and eighth weeks, and in the younger ones during the tenth week. At the final reading of the entire series, at the end of six months, induration was noted in 62 cases (30% of those available for inspection). At the end of the first year 154 (67%) out of the 229 cases still resident in the homes were inspected, and the results of this inspection are summarized in Table V.

TABLE V.—*Cosmetic Results with Vole Vaccine*

	1951 Series				1952 Series	
	After 1 Year		After 2 Years		After 1 Year	
	No.	%	No.	%	No.	%
A. Complete healing, with no residual marks	50	32·5	60	44·1	4	10·5
B. Small needle pricks (size of original ones) still seen (no induration)	20	13·0	14	10·3	11	28·9
C. As for B, but individual marks a little larger	66	42·9	30	22·1	19	50·0
D. Indurated arms	8	5·2	20	14·7	2	5·3
E. Complete healing, with residual scarring	10	6·5	12	8·8	2	5·3
Total	154		136		38	
Satisfactory ..		95%		89·7%		95%

It was noted that complete fading had occurred in 32.5%; almost complete fading in 13%; while in a further 42.9% the resultant scars were slight and could not cause any adverse criticism. In 88.4% the rosette had completely or almost completely disappeared. The 6.5% which showed scarring were not in any way unsightly, and our inspections have therefore shown that in almost 95% of the cases the late appearances of the vaccinations were satisfactory. In 5.2% of the cases, however, definite induration of the individual parts of the rosette was noted, and in 4% this was severe.

Inspection of the rosettes was repeated at the end of the second year and 136 arms were seen at this examination. The results are classified in Table V.

During the second year the proportion of arms with complete healing and no residual marks increased from 32.5% to 44.1%. Arms showing induration of the lesions rose from 5.2% to 14.7%, being slight in 4.4% but definitely unsightly in 10.3%. All these reactions were in children vaccinated by the multiple-puncture method. The term "induration" is used to describe local reactions of a lupoid character, varying from a few dry, indolent, crusted spots to a confluent, raised patch, similar in size to the area of the multiple-puncture gun. The increase in the proportion of lesions of this type between the observations made after one and two years was surprising and quite unexpected. Equally unexpected and disappointing was the fact that the appearances noted in arms showing marked induration at one year showed practically no change at the inspection at the end of two years. Several recorded at two years were seen in arms which had been regarded as healed at the end of one year and no explanation can yet be advanced to account for them. They are lupoid in appearance. While their cause is obscure we feel that trauma and possibly superinfection in the wide area of vaccination by the multiple-puncture gun are contributing factors. There has never been any suggestion of any lupoid reaction in any of the children receiving intradermal vole vaccine.

The 1952 series of vole multiple-puncture vaccinations were inspected at the end of one year, and the results were similar to those noted in the previous series. These late reactions are tabulated for comparison in Table V.

Discussion

After considerable experience with both methods we believe that multiple puncture has many advantages. There is no danger of injecting the vaccine at too deep a level, as may happen with the intradermal method in young and nervous children.

It is too early to draw firm conclusions on the results. Even though conversions take place more quickly with B.C.G. vaccine, the fact that by six to eight weeks the rates in the B.C.G. and vole are equal, and that conversions ultimately took place in 100% of our cases, indicated that the allergy produced is equally satisfactory with both vole and B.C.G. vaccines. When the reversion rates are considered there is no doubt that those relating to vole vaccine are more favourable. In our first series of cases, which have already been followed up closely for over two years, the proportion showing late lupoid reactions after multiple-puncture vole vaccine is, we consider, too high, and although the vaccine has distinct potentialities, we feel that it cannot be employed on more than an experimental basis until these difficulties have been overcome. We have noted that conversion always took place if any part of the rosette developed. We felt that satisfactory results could be obtained with half-strength liquid vaccine. The 1953 vaccinations were carried out to test this point, and so far we can report 100% conversion after six weeks.

All our 1951 cases have been followed up for over two years, and no case of tuberculous infection has yet been reported. One point which must be kept in mind is the definite loss of allergy after two years. What percentage of reversions can be expected after three, four, or five years? Any final comparison and decision regarding the merits of the vaccines must obviously await further testing of each of the three (and any other) groups over a further period of at least three to four years.

Summary

This report describes an investigation designed to compare vaccination with B.C.G. and vole bacillus vaccines, and records the preliminary results after one and two years. The B.C.G. was given in the routine intradermal manner and the vole vaccine by multiple puncture to those of 5 years and over and intradermally to those under 5 years. Vaccination by the multiple-puncture method is probably slower than by intradermal injection, but it is considered to be the method of choice and is simpler and more certain in young children.

The rate of conversion after vole vaccination is a little slower than after B.C.G., but the percentages—95% after six weeks and 100% after twelve weeks—are very satisfactory, and compare closely with those obtained with B.C.G.

We believe that vaccination with vole bacillus has certain advantages because of the milder clinical course and the smaller rate of reversions.

The periodic surveys showed that induration developed in a substantial proportion of the cases receiving vole vaccine by the multiple-puncture method, and that, later, lupoid reactions occurred in the vaccination area. These later complications were noted in 5% and 15% of the cases inspected after the first and second years. The discovery of lupoid reactions at the second yearly inspection in arms regarded as healed at the first yearly inspection was unexpected and unfortunate, and we regard the rate of these reactions to be too high to permit of the routine use of the vaccine until these difficulties have been overcome.

We are indebted to the Council of Management of the Orphan Homes of Scotland for permission to carry out the investigation; to Dr. J. S. M. Gray, County Medical Officer of Health, Renfrewshire, for help in carrying out the work; and to Professor F. R. G. Heaf, Dr. A. Q. Wells, and Dr. K. Neville Irvine for advice and assistance.

REFERENCES

Frew, H. W. O., Davidson, J. R., and Reid, J. T. W. (1953). *Brit. J. Tuberc.*, **47**, 68.

Wells, A. Q. (1946). *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, No. 259. London.

At the North of England Education Conference held in Sheffield on January 6, Mr. L. J. BARNES, director of Social Training at Oxford University, unfurled, in the words of the *Manchester Guardian* (January 7), "the banner of professional syndicalism." "We know," Mr. Barnes said, "that health centres don't exist because in the main the doctors don't want them." There was no evidence, however, of any opposition among teachers to county colleges. If the doctors wanted health centres they would get them; educationalists did not get county colleges whether they wanted them or not. The difference lay in the different types of professional organization in the two fields. The National Health Service, Mr. Barnes said, had come into being on the basis of professional syndicalism, subject only to parliamentary control. The doctors had managed it very cleverly and ingeniously, and he believed they were right to have done so. Professional syndicalism, subject only to lay control at the top, was the traditional pattern of the British public services; in education alone there was not yet any trace of it. "That fact is a great misfortune," Mr. Barnes concluded. "We shall never get anywhere in the field of adolescent education and welfare until the teaching profession takes effective steps in the direction of professional syndicalism."

TREATMENT OF PAPILLOMA OF BLADDER WITH RADIOACTIVE COLLOIDAL GOLD Au^{198}

BY

FRANK ELLIS, M.D., M.Sc., F.F.R.

AND

R. OLIVER, M.Sc., A.Inst.P., A.M.I.E.E.

(From the Department of Radiotherapy, Churchill Hospital, Oxford)

Villous papillomata of the bladder are usually multiple, and the possibility of distinguishing between benign and malignant tumours is an open question, both from the urologist's point of view, depending on interpretation of cystoscopic appearances at one and successive examinations, and from the point of view of the interpretation by the pathologist of the histological findings. In a proportion of patients papillomata in other situations, such as the larynx, breast, large intestine, and rectum, undergo malignant change, and it may be that villous papilloma of the bladder could correctly be regarded as a pre-malignant condition, as suggested by Riches (1948).

Buerger (1915) suggested that changes in size and staining properties, atypical mitoses, and multinucleate cells are evidence of malignant change. These changes would probably now be called "carcinoma *in situ*," but the further changes which he has described—invasion of the basement membrane and subsequent infiltration of the connective-tissue stroma of the papilloma and the presence of epithelial cells in the bladder wall and in blood vessels—are undoubted evidence of carcinoma. In 30% of 52 cases of carcinoma of the bladder reported by Buerger the carcinoma had been preceded by a papilloma. The true proportion of such malignant changes is masked by the fact that the papillomatous nature has been lost when a large, frankly malignant tumour is first found. These facts, and the fact that clinically benign and malignant papillomata often co-exist in the same bladder, accord with the view of Willis (1953) that pathological distinction between benign and malignant papillomata may be impossible.

Methods of Treatment

The treatment of these lesions by cysto-diathermy has for many years been the method of choice, but the results of such treatment are difficult to find. It is certain, however, that a number of patients develop incurable malignant disease after many years' cystoscopy and diathermy. Others may be cured by total cystectomy, which has been advocated as the treatment of choice even in relatively early cases. Total cystectomy, however, has a mortality and a morbidity which seem a high price to pay in the early cases.

X-ray treatment is used, but involves treating the whole bladder and some of the surrounding pelvic organs to a high dose of radiation.

The use of an intravesical rubber balloon containing radioactive solutions (Walton and Sinclair, 1952) or a central solid radioactive source emitting gamma radiation (Cones and Gregory, 1952) in a suitable balloon has also been tried, but, although the dose falls off relatively rapidly from the surface of such a balloon, the dose given to the subepithelial connective tissue is likely to be 70–90% of the dose to the bladder wall, and is likely to result in undesirable vascular and connective tissue changes which may, after some years, produce atrophic or metaplastic changes in the bladder epithelium.

Rationale of a New Method of Treatment

Because of these considerations, when presented with a patient suffering from haematuria due to myriads of papillomata covering the whole bladder surface, it was decided to explore the possibilities of using beta radiation to treat the papillomata. If the radioactive fluid could be used to fill the bladder without any containing balloon, the papillomata would float freely in it and be irradiated from all sides. The normal bladder wall, on the other hand, would be irradiated from only one aspect and the limited range of the beta emission would provide a very rapid fall in dose. Thus only the epithelium of the bladder would be treated and the subepithelial connective tissue would be almost unirradiated.

For such a method radioactive colloidal gold from A.E.R.E., Harwell, appeared to be the most suitable material available, since its beta emission (0.96 MeV) had a half-value layer of about 0.3 mm., which is comparable to the thickness of the papilloma as shown in Fig. 1, and its colloidal nature would militate against its absorption. It had the advantage that it could be introduced through a catheter, without opening the bladder, in a sufficient concentration to give a large enough dose of radiation during the relatively short time before the patient had to empty his bladder. It was estimated that some 300 mc. should be given in about 100 ml. of saline, so that, taking account of the dilution by urine passing into the bladder from the ureters, the dose to the bladder wall in two to three hours would be of the order of 3,000 r.

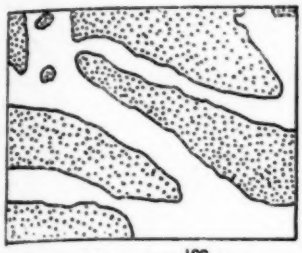


FIG. 1.—Relation of the half-value layer to thickness of the papilloma.

Preliminary Tests

Dangers in using such a large amount were anticipated from two points of view: (1) The absorption into the blood or lymph of 5 or 10% of such a large dose might have undesirable consequences. (2) The retention by sticking to the bladder wall of a relatively small amount could result in huge doses (about 1,000,000 r for 1 mc. per square cm.) of radiation to the bladder epithelium. (This had been found to occur in similar work with thorium-X before artificially produced isotopes were available. Thorium-X is an alpha-particle emitter with a range of only about 10 microns, however, and only beneficial results were observed.)

It was necessary to confirm that the colloid would remain in suspension while in the bladder. The solution is supplied slightly alkaline (about *p*H 8 in samples tested), and it was considered that the gelatin might become unstable and the colloid precipitate in acid conditions. Alkalination of the urine would prevent acidity in the bladder but lead to a large excretion, diluting the radioactive solution and limiting the maximum period of retention.

Actually a sample of inactive gold colloid was acidified with HCl to about *p*H 2 without any precipitation occurring immediately, on standing, or after incubation at 56° C. for about half an hour. Therefore 95 ml. of this inactive gold was introduced into a male patient's bladder through a catheter, which was then tied off. After two hours 340 ml. of fluid was drained off. The *p*H was only about 7 and no precipitation could be observed.

On the next occasion a similar volume of colloid was used with a total activity of about 400 μc. After two and a half hours 235 ml. of fluid was drained off and the bladder washed out three times with saline, each lot of fluid being retained. Also urine was collected for the next 12 hours. The activities of these samples, determined by comparison with a standard dilution from the original colloid, were 97%, 4.5%, 0.5%, 0.05%, and 0.05% respectively in fluid drained from the bladder, in the first, second, and third rinses, and in the urine. This total (102%) corresponded to the whole of the injected activity within the experimental accuracy. The gamma count rate over the bladder was not significantly above background, and a blood sample taken just before the bladder was drained showed no detectable activity.

Treatment

As these tests showed that the colloid was not precipitated in the bladder or absorbed, it was decided to proceed with treatment. Following cystoscopy, a Foley catheter was passed into the bladder. Three hundred mc. of radioactive colloidal gold in 100 ml. was taken into a syringe, a small sample was retained for making a standard dilution, and the rest was introduced into the bladder after the balloon of the Foley catheter had been inflated with 5 ml. of fluid. The end of the catheter was then securely tied off and the catheter fixed by strapping so that the balloon was used to close the neck of the bladder. After two and a half hours the bladder contents were drained off and the bladder washed out eight times with warm saline, by which time the washings were practically colourless.

The fluid and rinses were retained for activity measurements, and urine was collected for 24 hours. Care was taken to avoid leakage round the catheter and spillage of the active fluids during injection, draining, and rinsing. Gamma counter measurements were also made over the patient immediately and about 24 hours after the bladder was emptied. It was estimated that very much less than 0.5% of the injected gold was retained in the bladder and no other site of activity was observed. The dose received by the bladder epithelium was estimated to be 3,000 r (2,700 rep beta dose, 300 r gamma dose).

After two months the treatment was repeated, using an ordinary catheter, and a dose of about 2,400 r was delivered to the bladder wall.

When examined cystoscopically six weeks later, no papillomata could be seen except for a ring of small nodules around the internal urethral meatus where the contact of the Foley bag had protected them from the beta radiation. It was decided to treat these locally with radioactive cobalt so arranged in a Foley balloon at the neck of the bladder as to give a dose of 3,000 r, using a source–epithelium distance of 1 cm.

The patient is now well and symptom-free, and at his last cystoscopy, 15 months after the last treatment, his bladder wall was normal in appearance throughout. No other treatment has been given. The case summary is given below.

A man aged 67 was referred on September 8, 1952, by Mr. Till. He had had three weeks' haematuria in June, 1952, and occasionally since, and dysuria and nocturnal frequency since June, 1952: now D/N=3-hourly/2-hourly. Cystoscopy on August 29 had shown that the bladder was covered with villous papillomata, the main mass of growth being above the right ureteric orifice and around the left ureteric orifice.

October 10.—Biopsy: transitional-cell papilloma. Injection of non-radioactive colloidal gold into the bladder for two hours to test for possible precipitation. Blood: Hb, 81%, white blood cells, 5,000 per c.mm.

October 14.—110 ml. slightly active colloidal gold for two hours to ensure that no residual radioactivity remained after washing out the bladder.

October 18.—Radioactive colloidal gold, 377 mc. in 105 ml. for three hours. Total dose to surface, 3,000 r.

January 9, 1953.—Cystoscopy. Two papillomata: (A) above right ureteric orifice; (B) medial to left ureteric orifice; (C) fronds at bladder neck. Suggested diathermy of (A) and (B). Radium in Foley catheter to (C) and another treatment with colloidal gold.

January 27.—Coagulation of (A) and (B) (Mr. A. S. Till). Second injection of radioactive colloidal gold, 274 mc. in 100 ml. for three hours. Total dose to surface, 2,950 r.

April 14.—Radioactive cobalt in Foley catheter to treat neck of bladder, 3,000 r in 5 hours 20 minutes. Blood urea, 27 mg. per 100 ml.

June 16.—Cystoscopy. Redness of bladder wall. No neoplasm.

December 1.—Cystoscopy. Normal bladder mucosa. Symptom-free except for nocturnal frequency. The patient says this is a habit—he empties his bladder whenever he wakes up. Blood: Hb, 96%; white blood cells, 5,100 per c.mm.

April 20, 1954.—Symptom-free. Cystoscopy: normal bladder.

Suggested Routine

As a result of this treatment, experience has now been gained which makes it possible to recommend the following routine procedure in centres where the drill for the handling of isotopes is established.

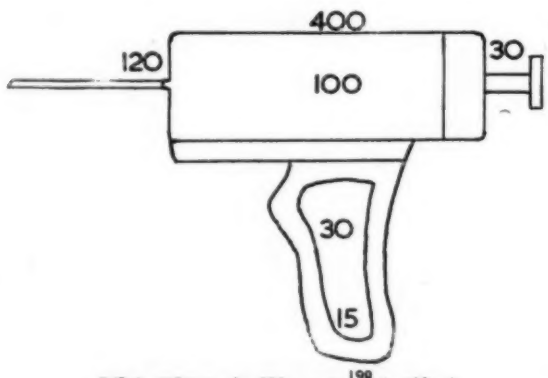
1. It is necessary to get the permission of the Medical Research Council to use the method.

2. After cystoscopic examination the plan of treatment of the case is decided, bearing in mind the morbid anatomy and pathology and the possible effects of the various surgical and radiotherapeutic steps in treating and possibly spreading the growth. For instance, in a recent case with multiple large malignant papillomata the plan decided upon was 3,000 r *x* rays (275 kV) to the bladder, 4,000 r with radioactive cobalt in a balloon introduced via a perineal urethrotomy, diathermy of any residues six weeks later, and then gold to be used only if seedlings began to develop subsequently.

3. Having decided to use the colloidal gold method, fluid intake is forbidden on the day of treatment. An ordinary rubber catheter of a large size is introduced, the bladder emptied, and the end of the catheter double tied. In females a purse-string linen suture is passed around the catheter at the external urethral meatus and tied tightly so as to prevent any risk of leakage.

4. Using the special protective gun (see Figs. 2 and 3) which has been made to enclose a 100-ml. syringe, some 300 mc. of colloidal gold is drawn into the syringe and made up to 100 ml. with saline.

FIG. 2.—Lead-protected gun for 100-ml. syringe.



D/R in MR/min. for 300 mc. Au^{198} in 100 ml.

FIG. 3.—Diagram of the syringe gun with 5-mm. lead protection.

5. The solution is injected, using a thin Record needle passed obliquely through the wall of the catheter.

6. Two samples of about 2 ml., one taken at the start and one at the end of the injection, are retained as standards for measurement of the activities of the fluid drained from the bladder and washes.

7. The patient is returned to the ward and put to bed. If he is active the solution mixes well with the urine passing into the bladder, but if he is sleepy following an anaesthetic it is necessary to move him about, tilting the bed and turning him on to his side so as to ensure mixing. This has been done because in one patient, who was asleep and stationary until the bladder was emptied, the bladder contents showed definite lack of mixing.

8. At the appropriate time (two and a half hours to three hours, determined as being likely with the dose used and the expected dilution to have given a dose of 3,000 r), with suitable precautions, the contents of the bladder are run off into a glass jar, and the bladder is washed out five or six times with warm saline into a succession of glass jars until the washings are free from the colour of the gold colloid.

9. The percentage of the gold in these washes is determined and the gamma-ray measurements are made over the suprapubic region with a counter, so as to determine if further washing is needed. This has not been necessary so far.

10. The urine is collected for 24 hours.

11. The dosage is estimated as described in the Appendix below.

Discussion

The points which it is required to know in connexion with any new method, apart from its rationale and technique, are: (*a*) if it is safe and if there are any untoward effects; (*b*) the type of case in which it is effective; and (*c*) other possible uses.

Safety

The method as detailed above has now been used on 22 occasions with no untoward effects on the patient and no suggestion of danger to staff. All patients have been sufficiently free of radioactive material and free of symptoms to leave hospital the next day.

Type of Case

(i) As previously indicated, the method was designed to treat cases of *multiple villous papillomatosis*. We have had only one such case referred. This has been described in detail above.

(ii) The method has been used also to treat the bladder in cases of papillomatosis with carcinoma. It is clear that the thickness of the tumour must determine the dose it receives, and so, when there are thick papillomata or a carcinoma, the dose received at a depth below the surface will be too small to be effective. Nevertheless, in some cases a rapid shrinkage may easily be obtained of part of a tumour, making easier a decision regarding subsequent treatment. This is illustrated by the following case summary:

A married woman aged 79 was referred by Mr. D. C. Corry on January 9, 1953. Her history was that she had the first attack of painless haematuria three years ago for two to three days and the second attack two weeks ago. She saw Dr. Wase after one week and continuously since.

January 5, 1953.—Cystoscopy. Papilliferous tumours of base of bladder obscuring both ureteric orifices. Suggested radioactive gold to clear the bladder and diminish the size of the tumour. Then Co^{60} balloon.

January 20.—Radioactive colloidal gold, 289 mc. in 86 ml. for three hours. Total dose to surface, 3,050 r.

February 24.—Cystoscopy. Tumour much smaller. Ureteric orifices seen. Three papilliferous tumours seen close to right ureteric orifice.

March 10.—Co^{60} in balloon. 5,500 r in ninety-three hours at 3.3 cm. distance.

May 1.—Cystoscopy. Tumours still smaller, but three papillomata still present.

August 14.—Cystoscopy. Biopsy of one lesion remaining just above right ureteric orifice. Transitional cell carcinoma—Broders's Grade 1.

August 21 to 28.—Treatment by uterine and vaginal radium to base of bladder—2,500 mg.hr. in uterus and 2,500 mg.hr. in vagina.

(iii) Treatment with radioactive colloidal gold has also been used as a method of treating the bladder to diminish the surface activity of a malignant growth three to four weeks before opening the bladder in cases in which cystostomy for implantation of radium, radon, or radioactive tantalum or for partial cystectomy was intended.

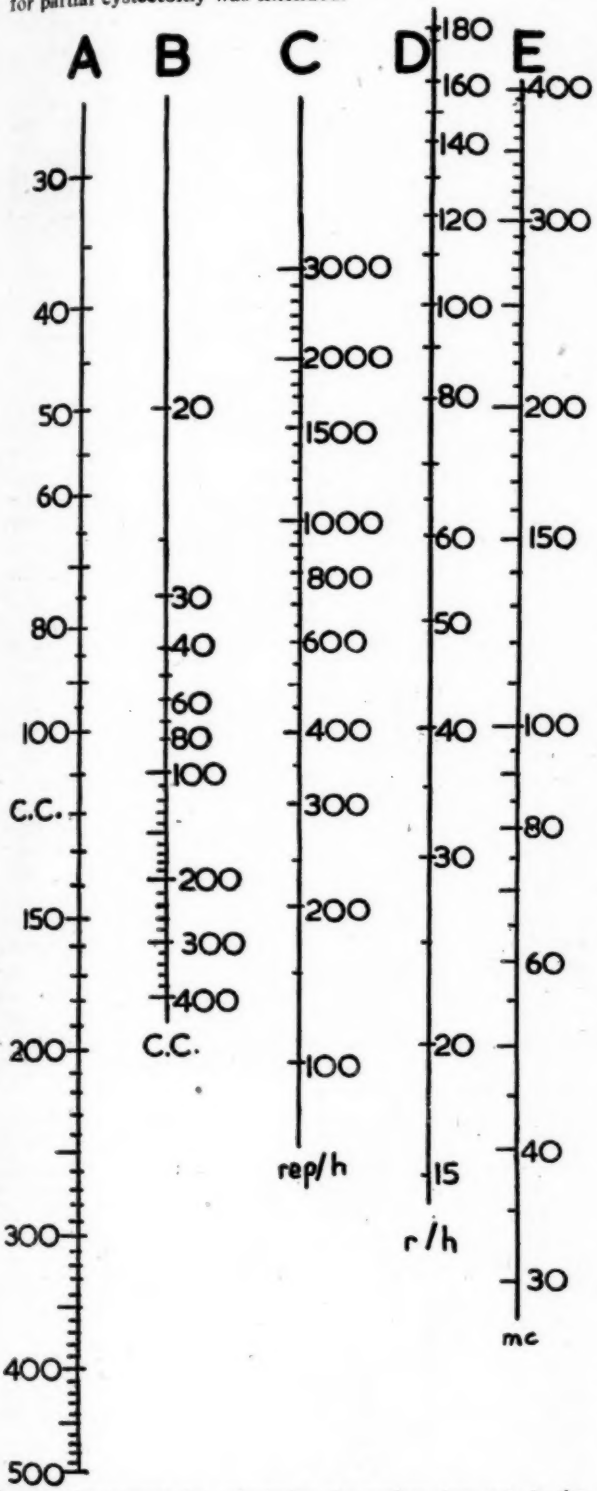


FIG. 4.—Nomograph for calculating the surface dose rate in the bladder. Read volume on "A" and mc. on "E" to give beta D/R on "C"; then from this value on "C" and volume on "B" read gamma D/R on "D."

(iv) It would theoretically be possible to treat with radioactive colloidal gold the pelvis of a kidney which is the seat of papillomata. However, it is doubtful whether accurate diagnosis of such cases or adequate follow-up afterwards will ever be possible.

Summary

A technique is described for the treatment of multiple villous papillomatosis of the bladder whereby some 300 mc. of radioactive colloidal gold (Au^{198}) may be introduced per urethram so as to deliver a dose to the bladder epithelium of about 3,000 r in three hours. The recommended course is two such treatments with about two months' interval.

The procedure is safe for the patient and for the staff, if properly carried out.

It has caused complete disappearance for fifteen months of myriads of papillomata in a 67-year-old man, leaving him symptom-free.

In cases unsuitable for complete treatment by this method it may be used to bring about the disappearance of multiple small tumours and to stop haemorrhage. Accurate cystoscopic examination may thereby be rendered possible and the surface of a carcinoma devitalized preparatory to subsequent cystostomy.

APPENDIX

Estimation of Dose.—Beta Dose: The maximum range of the Au^{198} beta particles is only some 3.8 mm., so that with any layer of active fluid of thickness greater than this the dose rate at the surface will be half that in an infinite medium and will be proportional to the specific activity. From data given by Marinelli, Quimby, and Hine (1948) the dose rate at the surface for an activity of 1 mc. per ml. would be 405 rep/h.* (340 rad/h.†). The depth dose will be small, falling to 50% at 0.3–0.4 mm. depth. **Gamma Dose:** Au^{198} also emits gamma radiation of 0.41 MeV energy, and the gamma dose rate at the surface will depend on both the specific activity and the dimensions of the cavity. If the bladder is considered as a sphere of radius r cm., the dose rate is given by 15.1 r (see Mayneord, 1950). This figure is based on a dose rate of 2.4 r/h. at 1 cm. from 1 mc. The depth dose here will be greater, but will have fallen to 50% at depths of 0.75–1.5 cm. for radii of 2.5–5 cm.

Deducting the volume of the catheter itself, the initial bladder volume is taken as equal to the volume of fluid injected, and the volume of fluid drained from the bladder is measured. It is assumed that urine drains into the bladder to increase the fluid volume at a constant rate, and the initial and final beta and gamma dose rates are calculated from the corresponding specific activities and volumes. The gamma dose rate does not, of course, increase linearly with volume, but, as this contributes only 10–15% of the total, the surface dose is given with sufficient accuracy from the average beta and gamma dose rates.

A nomograph for calculating these dose rates is given in Fig. 4.

We acknowledge the helpful co-operation of Dr. C. Lewis and Dr. P. J. van Miert in carrying out this technique, of surgical colleagues on the staff of the United Oxford Hospitals and Swindon Hospitals in referring patients for treatment, and of Mr. G. E. J. Jackson in the design and construction of the protected syringe gun.

REFERENCES

Buerger, L. (1915). *Surg. Gynec. Obstet.*, **21**, 179.
Cones, D. M. T., and Gregory, C. (1952). *Brit. J. Radiol.*, **25**, 597.
Marinelli, L. D., Quimby, E. H., and Hine, G. J. (1948). *Amer. J. Roentgenol.*, **59**, 260.
Mayneord, W. V. (1950). *Brit. J. Radiol.*, Suppl. **2**, 149.
Riches, E. W. (1948). *British Surgical Practice*, **2**, 140. Butterworth, London.
Walton, R. J., and Sinclair, W. K. (1952). *Brit. med. Bull.*, **8**, 158.
Willis, R. A. (1953). *Pathology of Tumours*, p. 467. Butterworth, London.

*1 rep=83.5 ergs/g.
†1 rad=100 ergs/g.

SPINAL DISK LESIONS

AN ASSESSMENT AFTER TWENTY-ONE YEARS

BY

JAMES CYRIAX, M.D., M.R.C.P.

Physician to the Department of Physical Medicine, St. Thomas's Hospital

"One-third of all orthopaedic out-patients complained of low backache. Had the panel any suggestion for coping with this vast number?

"They had none." (One of the questions put at the autumn meeting of the British Orthopaedic Association.)

In 1934 Mixter and Barr published their epoch-making paper describing relief from sciatica after the removal at laminectomy of part of a low lumbar disk. At the time the lesion was thought most rare, but in due course increasing experience enabled this diagnosis to be made more often. By ten years later the common cause of what had been called "sciatic neuritis" was beginning to be recognized as a low lumbar disk protrusion. Actually, Goldthwait (1911) had already ascribed lumbago and sciatica to disorders of the lumbo-sacral joint.

Cervical disk lesions soon came to the fore—the analogy was obvious—and by, say, 1950, root pressure from a cervical displacement was beginning to be widely regarded as a common cause of "brachial neuritis."

Thoracic disk lesions have only just begun to gain appreciable acceptance as the cause of "intercostal neuritis."

So much for root pain. But it had been known for centuries that lumbago often led to sciatica; that scapular "fibrositis" usually preceded brachial neuritis, and that "intercostal neuritis" might follow posterior thoracic pain. By 1950 the idea was gaining ground that lumbago was caused by internal derangement at a low lumbar level (Cyriax, 1945), and soon afterwards, that scapular and thoracic "fibrositis" might have their source in disk lesions at the relevant spinal levels (Cyriax, 1948). All this has now ceased to be particularly controversial, and the concept of a disk lesion causing pain solely in the trunk is already firmly established. Given that this is so, what effect has all this new knowledge had on the prescription of treatment? To-day, attending every hospital are large numbers of patients correctly diagnosed as suffering from disk lesions causing pain in trunk or limb. Is enough effort being made to employ effective measures on this large number of patients, some already severely disabled, and others in danger of such disablement unless given immediate attention? The answer is "no."

Cervical Disk Lesions

These usually present a unilateral scapular aching associated with pain on moving the neck. At this stage the displacement is small and immediate manipulative reduction succeeds in 99% of all cases, provided that general anaesthesia is avoided. One, seldom two, sessions suffice. Traction has been shown by radiography (Cyriax, 1954) almost to double the space at the intervertebral joint; strong manual traction is therefore maintained while the manipulations are carried out. Only slight discomfort is felt. This simple measure not only affords immediate relief from the scapular pain but prevents the later onset of brachial neuritis.

Occasionally a cervical disk protrusion causes central neckache or bilateral scapular discomfort, or bilateral brachial pain or paraesthesiae in the upper, lower, or all four limbs. In such cases immediate reduction is more important than ever; for any of these events implies that the protrusion is passing backwards in the midline. Since it has become evident that pressure from a central herniation on the spinal cord (Middleton and Teacher, 1911; Brain, 1954) and on the anterior spinal artery is responsible for cases hitherto diagnosed as amyotrophic lateral sclerosis or progressive muscular atrophy, it is reasonable to suppose that immediate reduction followed by its repetition whenever necessary may spare patients crippledom in later years.

Once root pain down the arm has begun, manipulative reduction is more difficult. When muscle paresis is absent, it remains successful in two-thirds of all cases; if a marked root palsy has supervened, failure is almost certain. The change from scapular discomfort to root pain may take years in one patient, hours in another. Hence there should be no delay; in each suitable case the manipulation should follow the establishment of the diagnosis within a few minutes.

Thoracic Disk Lesions

Whether causing posterior or anterior thoracic pain, a protrusion irreducible by manipulation during manual traction is a rarity. Should one be encountered, daily sustained traction seldom fails. By keeping the prevalence of thoracic disk protrusion in mind and examining the thoracic spinal joints for articular signs, the clinician can avoid many mistaken diagnoses of visceral lesions, hitherto obscure pain of months' or years' standing being found relievable within a few minutes. Moreover, since a thoracic protrusion can compress the spinal cord, reduction provides the prophylaxis of one cause of postero-lateral sclerosis and paraplegia.

At the thorax the maintenance of reduction is difficult. Lordosis is unobtainable; hence the patient must do his best not to stoop or lift; for eventual redisplacement is a virtual certainty. Manipulative reduction must then be repeated.

Lumbar Disk Lesions

These often start by causing chronic backache in women and attacks of lumbago in men. In the former case a small posterior displacement is present the whole time; in the latter the patient suffers bouts of acute lumbar pain and fixation caused by a major attack of internal derangement, but is symptom-free between-whiles. In backache, manipulative reduction, without anaesthesia, is usually successful; should it fail, sustained traction is called for. Between 100 and 200 lb. (45 and 90 kg.) is applied while the patient lies on a special couch for up to an hour daily. Manipulative reduction is also the treatment of choice in lumbago if the patient can bear it. If he cannot, epidural local analgesia is indicated; this abolishes the pain for one and a half hours, during which time he lies prone on a couch in hyperextension. The pain seldom returns to anything like its previous intensity.

Once reduction has been achieved redisplacement is obviated so far as is possible by postural instruction in the maintenance of lordosis and the provision, when necessary, of a corset or a plastic jacket. I have no patience with those who apply a plaster—belladonna or plaster of Paris—to the patient without reducing the displacement first. No one would dream of applying a plaster to a fracture without reducing it first, and, in my view, identical considerations apply at the lumbar spine.

When root pain has come on, reduction is often successful when straight-leg raising is limited but conduction is either not affected or only slightly. Should manipulation fail, traction is often quickly successful. Marked root paresis designates a protrusion too large ever to retrace its steps, but often implies an early cessation of pain; it is often best left alone. Primary postero-lateral herniations—that is, root pain without previous backache—in young patients are usually best left to recover spontaneously, with

or without the help of epidural local analgesia. Long-standing sciatica can sometimes be cured outright by one or two epidural injections.

When conservative treatment fails and the symptoms warrant, operation is indicated, but it is important not to confuse minor lesions in hypersensitive patients with major lesions. Laminectomy or arthrodesis is called for in 1 in 200 of the cases seen by me. It is difficult to escape the impression that, were conservative treatment on the lines set out above employed, many cases would not get to the point of laminectomy at all. Certainly many patients who had been considered unrelievable except by laminectomy have been found to respond satisfactorily and quickly to the above methods of conservative treatment.

Discussion on Treatment

Though the patient does not realize it, a disk lesion is a medical emergency. Future trouble is obviated so far as is possible if reduction can be carried out as soon as the diagnosis is established. Not only does the patient lose his symptoms there and then, but stretching of the posterior longitudinal ligament is reduced to a minimum. Since this ligament forms the only bar to further protrusion, every effort must be made to spare it the prolonged pressure of a continuing displacement, especially at the cervical and thoracic regions, where the spinal cord is in danger. Moreover, nearly all disk lesions set up pain in the trunk before the root pain supervenes; hence if reduction is carried out at this stage increased protrusion leading to root pressure is avoided.

This has been the policy for years at our physical medicine department. The methods are based on logic, are simple, and have proved effective. Manipulative reduction is usually carried out by the physiotherapy staff and students; they too attend to traction. My registrars and I give the epidural injections. In the last 17 years I have given some 15,000 such injections to unprepared out-patients without serious mishap.

The fact remains, however, that there is scarcely a hospital in the country where a minor disk subluxation is manipulated back into place while it remains minor and easy to reduce. Since patients with reducible displacement of part of a disk abound in every hospital, and the technique of reduction involves manipulation without anaesthesia, we have found that there is seldom any need for the doctor to give the treatment himself. This is delegated to trained personnel, and for the last 10 years our physiotherapists have carried out these manœuvres with manifest success.

The adoption of mechanical traction has proved less tardy, and within only five years of its advocacy for disk lesions (Cyriax, 1950) a number of hospitals have installed, or are considering installing, a traction couch. Epidural local analgesia appears everywhere unobtainable as an immediate out-patient measure. It is sad to reflect that these three main stand-bys of early treatment are not available to most sufferers. Only recumbency, a plaster jacket, and operation remain—all methods that, in my view, are called for only should the simple and quick methods fail.

But the patients know better. They go to the lay manipulator. And many medical men, knowing that neither themselves nor their hospital can help in such cases, recommend osteopathy. But why, when doctor and patient know that manipulation is the treatment of choice, is the patient forced to have recourse to a layman—not only that, but to pay him as well? Such a state of affairs would be unthinkable in any other branch of medicine and would not be tolerated for one moment were the displacement osseous. Yet a cartilaginous displacement requires reduction no less than a bony one. It is remarkable that this medical hiatus exists in the case of the spinal joints only—the very joints at which internal derangement is most frequent. The gift to the unqualified manipulator represented by this situation must astonish him; for great public esteem attaches to instantaneous relief from pain. Doctors thus render their own profession great disservice when the possessor of the common reducible disk lesion is left to wander to a layman.

Manipulation by Laymen

Neglect by medical men to consider manipulating a spinal joint, even after they themselves have stated internal derangement to be present, has created a group of laymen styling themselves osteopaths, chiropractors, and bone-setters. Patients do not wish to seek treatment outside the medical profession—even less so now, when they already pay the State for all medical care—but they discover that the appropriate treatment is not obtainable within the Service. So they *have* to go to a lay manipulator. And one must admit that, though devoid of diagnostic skill, such laymen often, in spite of not realizing the nature or the level of the lesion, relieve the patient immediately by a few simple manipulations. How easy it must therefore be for doctors or trained physiotherapists, with their anatomical knowledge, and basing themselves on a proper diagnosis, to do so too (Cyriax, 1949).

Were manipulation of the spinal joints restored to the medical sphere, not only would all suitable patients be relieved at once and the liability to further trouble be reduced to a minimum, but much abuse would be avoided, since the evil inherent in unsupervised recourse to laymen would cease—namely, repeated, fruitless, and expensive visits for conditions insusceptible to manual treatment.

Sooner or later, public agitation that spinal manipulation shall be obtainable within the Health Service will encourage the osteopathic fraternity to press again for State recognition. Luckily their fantastic claims put them outside the pale at the inquiry at the House of Lords in 1935. Let medical complacence not go too far; in Switzerland osteopaths are officially recognized, and in France osteopathy is a compulsory subject for medical students. The medical profession of Great Britain would be put in a most awkward position were another inquiry held to-day and the question asked of a number of hospitals—what arrangements exist in your out-patient department for spinal manipulation? Are the medical students shown, and the physiotherapy students at your school well grounded in, manipulation for disk displacement? It is no answer to say that manipulation is obtainable under anaesthesia by the orthopaedic surgeon on in-patients; this approach touches only the fringe of the problem, as the existence of some two thousand lay manipulators in this country demonstrates. The orthopaedic surgeon has many far more important operations to perform and, with the best will in the world, cannot deal with more than a tiny fraction of suitable cases, even if the beds were available.

Medico-legal Aspect

This has its anxious side. When a patient consults a medical man and is found to have a fracture out of alignment, a dislocated bone, or a displaced cartilage at the knee, reduction (usually by manipulation) is the accepted treatment. Were no effort made to reduce the displacement, or a good reason for refraining not set out, the attending practitioner might well find himself in medico-legal difficulty. In these times of increasing litigation it will not be long before some enterprising patient, after he has developed a major disk lesion, points out that, when he first consulted his doctor, the displacement was slight and that no effort at reduction was then made. Moreover, it may well happen that after various medical men have been consulted—and it is agreed by all that a displacement is present—the patient gives way to his friends' exhortations and visits a lay manipulator, who may afford him immediate relief. The patient can now argue very plausibly that he had an easily reducible disk lesion but that none of those whom he consulted treated him skilfully. This might be construed as negligence, not on the part of the general practitioner, but on that of any consultant he may have seen. In my

view the time is not far off when the illogical but time-honoured attitude of leaving a minor disk lesion to get larger or smaller as fortune dictates will provide us with another legal hazard.

Economic Considerations

If a family doctor is asked how many patients in bed with lumbago he has at any one moment, the usual answer is one, two or three. This implies that between 20,000 and 50,000 patients are off work at any one time because of a displaced fragment of disk. Were patients off sick because of a stiff neck, brachial neuritis, "fibrositis," pleurodynia, and sciatica all added to the list, a huge total of largely avoidable disablement would be reached. This costs the Health Service in sickness benefits far more than the expense that would be entailed in securing adequate treatment for the sufferers. Without further research, merely by a more general application of methods already evolved and continuously tested since, a great saving in pain and disablement would accrue, with huge advantage to the financial aspect of health insurance. From the economic point of view it is the logical treatment of the common disorders of the vertebral column that would make the biggest immediate contribution to industrial health to-day.

Summary

The rediscovery 21 years ago of intervertebral disk lesions explains the cause of many pains in the trunk and limbs, previously misunderstood. This clarification has not been followed by enough change in methods of treatment. Measures thought appropriate in previous decades—for example, heat, massage, exercises—remain in use at a time when reduction by manipulation or traction is required.

At present spinal manipulation for disk lesions is largely in the hands of laymen. This is a sad state of affairs; for if a patient requires treatment for an intervertebral displacement this should be administered by a doctor; failing that, by a physiotherapist working under his direction. The economic benefit is no less important than the humanitarian aspect.

Physiotherapists should be trained in accurate manipulation and thus make treatment for the reducible disk lesion possible on a large scale within the Health Service. It can be done, as our experience at St. Thomas's Hospital proves, and would render lay manipulators superfluous.

REFERENCES

Brain, R. (1954). *Lancet*, **1**, 687.
Cyriax, J. (1945). Ibid., **2**, 427.
—— (1948). *British Medical Journal*, **2**, 251.
—— (1949). *Osteopathy and Manipulation*. Lockwood, London.
—— (1950). *British Medical Journal*, **2**, 1434.
—— (1954). *Orthopaedic Medicine*, vol. 1, plates 5 and 6. Cassell, London.
Goldthwait, J. E. (1911). *Boston med. surg. J.*, **164**, 365.
Middleton, G. S., and Teacher, J. H. (1911). *Glasg. med. J.*, **76**, 139.
Mixter, W. J., and Barr, J. S. (1934). *New Engl. J. Med.*, **211**, 210.

The Association of Universities of the British Commonwealth has just published, as a pamphlet entitled *United Kingdom Postgraduate Awards (Fellowships, Scholarships, Grants, etc.)*, Appendices II and III of the *Commonwealth Universities Yearbook, 1955*. The *Yearbook* itself will be published in May. Appendix II contains a list of post-graduate awards "for advanced study and research tenable in the United Kingdom." It has been prepared as the result of a resolution of the Congress of Universities of the Commonwealth that each of the countries of the Commonwealth should draw up a list of postgraduate and research awards available at its universities for overseas graduates. Appendix III contains a list of postgraduate and research awards tenable outside the United Kingdom. It applies only to United Kingdom graduates and does not claim to be exhaustive. The pamphlet can be obtained from the secretary, Association of Universities of the British Commonwealth, 36, Gordon Square, London, W.C.1.

PRIMARY TUMOURS OF THE SMALL BOWEL

BY

T. A. OGILVIE, M.B., F.R.C.S.Ed.
Surgeon, Essex County Hospital, Colchester

AND

H. M. SHAW, M.B., F.R.C.S.
Registrar, Essex County Hospital, Colchester

It is now well recognized that tumours of the small bowel, though rare, account for about 3% of tumours found in the gastro-intestinal tract, and that most surgeons will encounter several in the course of their career. The incidence of tumours of the small bowel is greatest in the duodenum. Willis (1948), quoting a series published by Hoffman and Pack (1937), mentions that, of 228 small-bowel tumours, 104 were situated in the duodenum. As the distance along the small bowel from the duodeno-jejunal junction increases so the incidence of tumours decreases, the symptomatology is different, and there are types of neoplasm met with in the jejuno-ileum seldom seen in the duodenum. One may therefore consider the two categories, duodenal and jejuno-ileal neoplasms.

Tumours of the small bowel are of four main types and may be innocent or malignant:

Types of Small-bowel Tumour

	Innocent	Malignant
I. Epithelial tumours ..	Adenoma	Adenocarcinoma
II. Connective-tissue tumours	Fibroma, myoma, lipoma, neuro-fibroma	Fibrosarcoma, leiomyo-sarcoma
III. Tumours of lymphatic or vascular origin	Angioma	Lymphosarcoma, reticu-lum-cell sarcoma, Hodg-kin's disease
IV. Special group ..		Carcinoid

In general, it may be said that these tumours produce symptoms in one of four ways: (1) Obstruction, which may be due to an annular stricture, to intussusception with the tumour at the apex, or to volvulus. (2) Jaundice due to obstruction at the ampulla of Vater. (3) Melaena, anorexia, and loss of weight. (4) Perforation, which is a rare method of presentation.

It is not intended to discuss the signs and symptoms in detail, but rather to present the experience gained at a provincial hospital in dealing with these tumours over a period of ten years. In this period 16 cases have been diagnosed as suffering from small-bowel neoplasms. The details of these cases are shown in the table on the opposite page.

If we consider these cases together it will be seen that 12 presented with symptoms of acute or subacute small-bowel obstruction, 2 with abdominal discomfort and jaundice, and 2 with abdominal discomfort and melaena. In most of these cases pre-operative investigation was of little help in establishing the diagnosis, as in many of them operation was performed forty-eight to seventy-two hours after admission for the relief of obstructive symptoms. However, in four cases a barium meal examination was made, but was negative in each instance. The benzidine test for occult blood was performed in four cases and in each case gave a positive result. A plain film of the abdomen with the patient

standing in order to demonstrate fluid levels was done in six cases, and in none of these were fluid levels seen. Other investigations included barium enemata and sigmoidoscopy in isolated instances with negative results. All the diagnoses were confirmed by section of material removed at operation or at post-mortem examination. We shall now consider these lesions individually in more detail—8 carcinomata, 5 sarcomata, 1 argentaffinoma, and 2 benign tumours.

Carcinoma

Adenocarcinoma of the small bowel may affect the duodenum or the jejuno-ileum, though it usually appears not more than 2 feet (60 cm.) from the duodeno-jejunal junction (Ewing, 1940); although in a series published by the Mayo Clinic (Mayo, 1940) there were 31 tumours in the jejunum and 21 in the ileum. Of those arising in the duodenum, 22.5% are situated above the ampulla of Vater, 59.2% are peri-ampullary, and 18.3% are situated below the ampulla, these figures being given in a review of the subject by Locke (1953). Those growths situated around the ampulla of Vater may in fact be arising from the lower end of the common bile duct, and it is very difficult in many cases to decide whether they are duodenal or ampullary in origin: in advanced cases it may even be difficult to decide whether the tumour arises from the duodenum or the pancreas. Adenocarcinoma of the small bowel may be proliferative, may form an ulcer or an annular stricture, or may be a mixture of these varieties. Symptoms will depend on the site and type of growth present. Lesions of the duodenum are often associated with obstructive jaundice; ulceration produces melaena, and obstruction when it occurs is late. Ulcerating lesions in the jejuno-ileum may produce melaena, but obstructive symptoms are also late owing to the fluid nature of the small-bowel contents. Vomiting is more pronounced in duodenal than in jejuno-ileal lesions. The diagnosis in these cases may be helped by straight *x*-ray examination of the abdomen, which will sometimes show fluid levels above the site of the lesion. Barium meal and follow-through is sometimes of use, and is safe if a Miller–Abbott tube be first passed down to the site of the obstruction. Barium studies may show a filling defect, an ulcer, or annular constriction at the site of the lesion. In cases in which ulceration has occurred the benzidine test on the stool should be positive.

In our series there are eight adenocarcinomata, situated as follows: second part of duodenum—peri-ampullary, 3; duodeno-jejunal junction, 1; proximal jejunum, 3; terminal ileum, 1.

Of the three tumours in the duodenum, two were associated with obstructive jaundice and subacute bowel symptoms of an obstructive nature. The only symptom associated with the third case was the recent appearance of an epigastric mass in a person who had had steatorrhoea for years. Case 6 is interesting because of its mode of presentation and subsequent history.

Case 6.—A woman aged 61 was admitted in December, 1951, complaining of jaundice for three months which was becoming progressively worse. Her urine was dark and the stools were clay-coloured. There was no other relevant history. On examination she was seen to be an obese, markedly jaundiced, middle-aged woman. Abdominal palpation revealed a moderately enlarged liver, but the gall-bladder was not palpable and no other abnormality was detected. Biochemical investigation indicated that her jaundice was of an obstructive type, and straight *x*-ray examination of the abdomen, including the gall-bladder area, was negative. Laparotomy was carried out in December, 1951: the gall-bladder was dilated and a firm mass was felt in the head of the pancreas. No glands were palpable and there were no secondaries in the liver. A duodenectomy and removal of the head of the pancreas were done in one stage, but section showed the tumour to be a papillary adenocarcinoma of the duodenum. Convalescence was uneventful, and she remained well until June, 1953, when multiple pulmonary metastases were demonstrated.

Details of Cases

Case No.	Date	Sex and Age	Symptom	Duration	Operative Finding	Section	Result
1	18/2/51	F 82	Colicky abdominal pain	2 months	Carcinoma terminal ileum. R. hemicolectomy	Adenocarcinoma	Death, 28/5/52
2	26/1/52	F 19	Recurrent abdominal colic	1 month	Laparotomy. Reticulosarcoma. Biopsy gland	Reticulosarcoma	Untraced
3	Feb., '47	M 50	Abdominal pain—colic. Vomiting	4 days	Carcinoma jejunum. Resection and anastomosis	Adenocarcinoma	Secondaries. Death, Dec., '47
4	28/12/51	F 76	Jaundice. Vomiting. Abdominal pain	6 weeks	Laparotomy. Carcinoma ampulla of Vater. Cholecystostomy	P.M.: carcinoma of ampulla	Death, 3/1/52
5	13/12/51	M 38	Abdominal discomfort. Vomiting	1 week	Laparotomy. Chylous ascites. Thickened rigid bowel. Mesenteric glands enlarged—grey	Reticulosarcoma	Death
6	12/12/51	F 61	Painless obstructive jaundice	4 months	Hard mass 2nd part duodenum. Duodenectomy and removal head of pancreas	Adenocarcinoma duodenum	Alive. Pulmonary secondaries
7	3/8/50	F 33	Colicky abdominal pain	3 ,,	Multiple tumours ileum; glands	Argentaffin carcinoma	Alive
8	4/5/50	M 5	Abdominal pain. Vomiting	2 weeks	Chylous ascites. Bowel thickened. Liver, spleen enlarged. Mass in pouch of Douglas	Lymphosarcoma	Death, 8/5/50
9	20/9/50	F 30	Recurrent colicky abdominal pain	3 months	Intussusception. Adenoma ileum	Adenoma	Alive
10	29/12/50	M 33	Abdominal colic. Haematemesis	4 days	Subtotal gastrectomy	P.M.: lymphosarcoma involving stomach and small bowel	Death
11	28/10/51	F 48	Repeated melaena. Epigastric pain	6 months	? Carcinoma pancreas. Duodenectomy and partial pancreatectomy	Polypoid carcinoma duodenum	,,
12	3/5/50	F 50	Generalized abdominal pain. Melaena	4 weeks	Resection of terminal ileum with Meckel's diverticulum and leiomyoma	Leiomyoma	Alive
13	Sept., '48	F 65	Abdominal pain. Constipation	2 months	Carcinoma jejunum 4 in. from duodeno-jejunal flexure. Glands++. Resection and anastomosis	Reticulosarcoma	Death
14	21/1/53	M 40	Steatorrhoea for years. Abdominal discomfort	3 ,,	Carcinoma duodeno-jejunal junction. Resection and anastomosis	Adenocarcinoma	Death. Thrombosis superior mesenteric artery
15	10/1/46	M 50	Colicky abdominal pain	2 weeks	Carcinoma jejunum 2 in. beyond duodeno-jejunal junction. Glands++. Gastro-enterostomy	P.M.: adenocarcinoma	Death
16	19/8/52	F 44	Recurrent attacks of colicky abdominal pain. Vomiting	3 months	Annular carcinoma jejunum 12 in. from duodeno-jejunal junction. Glands++	Adenocarcinoma	Readmitted June, 1953. Large mass in pelvis. Laparotomy. Krukenberg tumour right ovary

All the growths in the jejunum and ileum were associated with obstructive symptoms varying from 2–3 days to 2–3 months in duration. In each case laparotomy was performed shortly after admission. Case 3 is illustrative.

Case 3.—A man aged 50 was admitted to hospital in February, 1947, complaining of colicky abdominal pain of four days' duration; there was no vomiting. His abdomen was slightly distended and he was tender to the left of his umbilicus. His symptoms subsided with expectant treatment but recurred at intervals until April of that year. A test for occult blood was positive, but barium enema and sigmoidoscopy were both negative. Haemoglobin was 94%. In April a tender mass was noticed in his left iliac fossa and laparotomy was performed. He was found to have an annular carcinoma of the jejunum approximately 2 ft. (60 cm.) from the duodeno-jejunal flexure, and this had led to a small-bowel volvulus. Secondary glands were felt in the mesentery and peritoneal deposits in the pelvis. The affected portion of bowel was resected and an end-to-end anastomosis performed. Convalescence was satisfactory, but he died from secondary carcinomatosis in January, 1948.

The duodenum and jejuno-ileum both have an abundant lymphatic drainage, together with a rich blood supply, and this probably accounts for neoplasms of the small bowel tending to metastasize early to the mesenteric lymph nodes and to the liver. Lesions in the duodenum produce symptoms at a rather earlier stage than do those in the jejuno-ileum, even before any metastases have occurred. The treatment of choice is resection of the involved segment together with its lymphatic field, followed by end-to-end anastomosis. General experience has shown these lesions to have a very poor prognosis, symptoms severe enough to cause the patient to seek treatment not occurring until comparatively late in the disease. This is borne out by our cases.

The Sarcoma Group

Amongst our cases there were five which came within this category. Two of these patients, aged 5 and 33, were diagnosed as suffering from lymphosarcoma, while three, aged 65, 38, and 19, were shown to have a reticulum-cell sarcoma. These two diseases together with Hodgkin's disease may primarily involve the mesenteric lymph nodes and lymphatic tissue in the wall of the small bowel. They frequently cause a chylous ascites due to lymphatic obstruction. The peritoneum may be studded with firm greyish nodules of tumour tissue. Large masses may be produced by glandular enlargement and the matting together of thickened and rigid loops of small bowel, resulting in subacute small-bowel obstruction. In some of these cases the liver and spleen may be involved. Diagnosis is often difficult, though the presence of an enlarged liver or spleen or of glands elsewhere may help, but in the present series the child of 5 was the only patient with a palpable liver and spleen. Full blood examination and glandular biopsy will help in establishing the diagnosis. One patient had previously been admitted elsewhere with a haematemesis for which he had undergone partial gastrectomy before the correct diagnosis was reached. In Cases 2, 8, and 13 there was a palpable mass in the lower abdomen. In all cases, at laparotomy, a large mass was found involving both the wall of the small bowel and its mesentery. In suitable cases resection of the involved segment followed by radiotherapy would appear to be the treatment of choice, although in none of our cases was this possible. Case 2 demonstrates these points.

Case 2.—A girl of 19 was admitted to hospital on January 26, 1952, having had an attack of severe colicky upper abdominal pain. Prior to admission she had had frequent attacks of less severe pain, each associated with vomiting. Bowel and urinary history were normal, menstruation was trouble-free. On examination there was an ill-defined lower abdominal tumour, but no other abnormality was noted. Laparotomy was performed on January 29, when the peritoneal cavity was found to contain a large quantity of chylous fluid. The mesentery of the terminal ileum together with the bowel itself formed a large mass. There were numerous grossly enlarged glands, the lymphatics were dilated, and there were several large lymphatic cysts, some 3 in. (7.5 cm.) in diameter, along the mesenteric border of the bowel. The bowel itself was thickened and rigid. It was only possible to remove a gland for biopsy, and the report was as follows: "Great increase of reticular elements at the expense of lymphoid tissue in the gland. No normal lymphoid follicles seen. Probably a reticulosarcoma." There is no record of this patient having been seen since at the hospital.

The prognosis in these cases is that of the general disease, and, as is well known, is uniformly poor. Fibrosarcoma and leiomyosarcoma may both occur in the small bowel but have not been met with in this series.

Carcinoid Tumours or Argentaffin Carcinoma

These deserve special mention, occurring as they do in two special situations, the appendix and the terminal ileum.

These tumours arise from granular cells lining the depths of the crypts of Lieberkühn. They were described by Kultschitzky and have a special staining reaction with silver stains, thus often being referred to as argentaffin cells. Freidin (1953) states that these tumours occur as a result of abnormal proliferation of the argentaffin cells, the tumour first appearing in between mucosa and the muscularis mucosæ and forming a yellowish-white mass over which the mucous membrane is stretched. As the mass increases in size it comes to involve the serosal surface of the bowel, where it may be seen as a yellowish or greyish plaque which, as a general rule, does not completely encircle the bowel, and thus obstruction may not be a prominent feature. The mucous membrane seldom becomes ulcerated over the tumour. Microscopically, the tumour is made up of columns of round or polyhedral cells with a granular cytoplasm and a darkly staining nucleus. There is no attempt at gland formation.

Tumours in the appendix are characteristically single and most frequently occur near the tip: they are usually discovered following routine appendicectomy or at necropsy. Ileal growths may be multiple, but, as they may not always encircle the bowel completely, symptoms may be absent. In his series Freidin reports that 13 of 16 ileal carcinoid tumours were found incidentally at post-mortem examination, the others causing obstructive symptoms. Metastasis from appendical lesions is seen in about 5% of the cases. Metastasis from ileal lesions is more frequent, and secondary deposits are found in the regional lymph glands and in the liver. Though similar in appearance and in microscopic structure, appendical and ileal lesions have several important differences which are summarized below, the figures being taken from Freidin's series of 30 cases.

	Appendix	Jejuno-ileum
Sex incidence	M:F=4:10	M:F=14:2
Age	Average 26 years	Average 26 years
Number	Single	May be multiple
Metastasis	Rare	Common

One of our cases (No. 7) is worth reporting.

Case 7.—A married woman aged 33 was admitted to hospital on August 3, 1950, complaining of lower abdominal pain of a colicky nature which had been present for three months. A straight *x*-ray film of the abdomen and a barium meal and follow-through showed no abnormality. Laparotomy was carried out on August 4 and in the ileum 17 isolated yellowish-coloured tumours were found almost completely encircling the bowel. The mesenteric glands were enlarged with similar growth and there were peritoneal seedlings. Approximately 8 ft. (2.4 metres) of ileum containing these tumours together with the mesentery and as many glands as possible were removed and an end-to-end anastomosis was performed. Convalescence was uneventful and the patient was alive and well three years after operation.

This case is remarkable in that there seems to have been no progression of secondaries in the three years since operation.

Benign Tumours

Many types of benign tumours may occur in the small bowel from time to time, and in this series we have two such cases. The first of these was an adenoma situated in the terminal ileum and forming the apex of an intussusception in a woman aged 30. The intussusception was reduced and the adenoma removed. The patient was still alive and well at the time of writing. The second tumour occurred in a

woman aged 50 who presented with melaena. Laparotomy showed her to have a Meckel's diverticulum and a rounded tumour in the wall of her terminal ileum distal to the diverticulum. Resection of the involved segment of ileum was carried out, section showing the tumour to be a leiomyoma.

Summary

We have reviewed briefly the primary tumours met with in the small intestine and report a series of 16 such tumours dealt with in this hospital over the past ten years.

Adenocarcinoma is the commonest of these tumours. It occurs most frequently in the duodenum and upper jejunum. Symptoms occur late owing to the fluid nature of the bowel content at this level. Prognosis is uniformly poor, and this has been our experience. The age incidence of these growths corresponds to the general cancer age, and women were affected more often than men.

A description of the lesions produced by lymphosarcoma and allied conditions is given. Five such cases are reported, and it is suggested that in suitable cases resection of the involved segment followed by radiotherapy is the treatment of choice.

A description is given of the carcinoid or argentaffin carcinoma. The different behaviour of this tumour occurring in the appendix and ileum is discussed, and one such case is reported.

Our thanks are due to other members of the staff of the Essex County Hospital for allowing access to their case records, and to Dr. J. B. Penfold for his helpful criticism.

REFERENCES

Ewing, J. (1940). *Neoplastic Diseases*, 4th ed. Saunders, Philadelphia.
Freidin, J. (1953). *Aust. N.Z. J. Surg.*, **22**, 231.
Hoffman, W. J., and Pack, G. T. (1937). *Arch. Surg. (Chicago)*, **35**, 11.
Locke, D. J. (1953). *Amer. J. Surg.*, **85**, 127.
Mayo, C. W. (1940). *West J. Surg.*, **48**, 406.
Willis, R. A. (1948). *Pathology of Tumours*. Butterworth, London.

ASSOCIATION OF JEJUNAL DIVERTICULOSIS AND STEATORRHOEA

BY

A. P. DICK, M.D., F.R.C.P.

(From Addenbrooke's Hospital, Cambridge)

It seems justifiable to report the following single case of steatorrhoea, macrocytic anaemia, and glossitis associated with multiple jejunal diverticulosis, in view of the considerable theoretical interest of the association and the apparent rarity of the occurrence. No similar case can be found in the literature. Moreover, the diarrhoea was relieved for a period of eight months after a course of chlortetracycline ("aureomycin"), and during this time the anaemia remained in remission without other treatment.

Diverticula of the small intestine between the duodeno-jejunal flexure and the ileo-caecal valve are usually symptomless and are found by chance in the course of a barium-meal examination or at necropsy. Their incidence has been recorded as 9 cases in 2,820 necropsies at King's College Hospital and as 0.31% by Edwards (1939), but it may be commoner than this. Benson, Dixon, and Waugh (1943) state that 122 cases had been recorded at the Mayo Clinic, of which 100 were jejunal, 17 in the ileum, and in 5 cases the diverticula were present in both. They are commoner in older people (Edwards, 1939). They are said on occasion to give rise to vague abdominal symptoms such as flatulence and postprandial discomfort, but in some instances it may be that the presence of these symptoms from other causes has led to the performance of a barium meal and the discovery of the diverticula.

Complications such as acute intestinal obstruction, volvulus in relation to diverticula (Stiven, 1934), haemorrhage (Braithwaite, 1923; Waterson, 1952), perforation (Butler, 1937), diverticulitis (Butler, 1933), and the syndrome of chronic intestinal obstruction (Phillips, 1953) have all been described. The latter consists of symptoms varying from vague abdominal discomfort to more definite colic, vomiting, and constipation with loss of weight and deterioration in general health. Phillips, in discussing this syndrome, points out that there is no organic obstruction at laparotomy, although distended hypertrophic loops of bowel may be found, and he in fact suggests that there is a "dyskinesia" of the bowel which produces this syndrome and which also causes the pulsion-diverticula. He quotes Benson *et al.* (1943) as stating that non-organic chronic small-bowel obstruction was the commonest observed complication in their series of 122 cases—and that the changes resemble those in small intestine which has been obstructed for a long period. One of two cases which he describes had loose stools.

No reference to their association with deficiency syndromes from failure of small-intestinal absorption can be found in the literature other than a single case report by Montuschi (1949). He reported the case of a man aged 66 with a history of eight years' recurrent abdominal pain and bouts of diarrhoea and four years' oedema of the legs. Investigation showed a lowered plasma albumin and a raised faecal fat. Barium examination revealed multiple diverticula in the small intestine and colon, with precipitate passage of barium through the small intestine and loss of the normal mucosal pattern. It was thought that a low-grade inflammatory process in the diverticula was probably the cause of the small-intestinal hurry which led to deficient absorption of protein.

Case Report

A housewife aged 71 was first seen in December, 1949. She had been in good health until five years previously, when she began to have two or three loose motions a day, the stools being sometimes pale. She did state that her bowels had always tended to be easily upset, but that it was seldom this occurred. Three years before she developed a sore tongue, and shortly afterwards in November, 1946, a blood count showed some macrocytosis and anisocytosis. (Details of blood counts are given in the Table.) On December 20 a barium meal showed a small hiatus hernia. On the second part of the duodenum and on the duodeno-jejunal flexure there were large diverticula, and there were multiple diverticula throughout the jejunum. These showed some stasis in the erect position (Dr. F. R. Berridge). She was apparently diagnosed as suffering from pernicious anaemia, and it was thought that the diarrhoea was due to achlorhydria.

She was treated with a purified liver extract ("anahaemin") intramuscularly once a fortnight at first, and subsequently monthly for the next three years until she was admitted to hospital. No test meal had been done. Full particulars of her blood counts during this time are not available, but she still had macrocytosis in 1949. Her diarrhoea remained unchanged during this time, and her tongue continued to be sore most of the time, with occasional periods when it did not trouble her. One month before admission she developed much more severe diarrhoea, having 10 watery stools a day and copious vomiting. The

Treatment:	Anahaemin i.m.						Ascorbic Acid, Vit. B, Folic Acid		Nicotinic Acid, Riboflavine, Vit. B, Folic Acid	Folic Acid	Admission 27/11/50–9/12/50	Plexan, 4 ml. i.m. Weekly
	Nov. 1946	Jan. 1947	May '47	6/1/49	30/12/49	10/1/50	20/1/50	3/2/50	17/3/50	14/7/50		27/12/50
R.B.C. (mills) ..	4·12	4·15	5·12	4·11	3·64	3·67	3·81	3·7	4·37	4·66		3·76
Hb (g.%) ..	15·6	14·1	15·6	14·0	12·8	11·7	13·4	14·0	14·5	15·1		14·0
M.C.H. (γγ) ..	38·0		30·5	34·1	35·2	31·9	35·0	38·0	34·0	32·5		37·3
M.C.V. (cubic μ) ..				109·3	107·2	100·5	110·0	117·0	102·0	94·0		109·6
M.C.H.C. (%) ..		34·0		31·1	32·7	31·6	31·8	32·2	32·4	34·4		34·1
Reticulocytes (%) ..					Less than 0·5		0·5	1·3	0·1	1·4		
W.B.C.	4,000			Normal	Normal	Normal	Normal					
	Macrocytosis. Anisocytosis			Some macrocytosis	Macrocytosis. Anisocytosis	Normochromia. Some macrocytosis			Anisocytosis +	Anisocytosis +		Normochromia. Anisocytosis. Macrocytosis

Treatment:	Plexan, 4 ml. i.m. Weekly	Plexan, 4 ml. i.m. Fortnightly					Chlortetracycline. Total in 9 days =9·25 g.	No Treatment			
	26/1/51	25/5/51	17/8/51	1/2/52	2/5/52	6/2/53		10/7/53	16/10/53	15/1/54	23/4/54
R.B.C. (mills) ..	13·8	15·0	4·76	4·87	4·79	4·53		4·75	4·8	4·73	4·2
Hb (g.%) ..			13·3	14·5	13·6	14·8		13·6	14·0	14·0	13·5
M.C.H. (γγ) ..			28·0	29·8	28·4	32·7		28·6	29·2	29·6	32·1
M.C.V. (cubic μ) ..			88·5	88·5	90·8	99·3		88·5	87·7	91·0	95·0
M.C.H.C. (%) ..			31·8	33·7	31·3	32·9		32·3	33·4	32·6	33·8
	Normochromia. Some anisocytosis	Normochromia. Normocytosis	Normochromia. Normocytosis	Normochromia. Some anisocytosis	Normochromia. Normocytosis	Normochromia. Anisocytosis		Normochromia. Some anisocytosis	Normochromia. Anisocytosis		Normochromia. Anisocytosis

diarrhoea lasted for 14 days, and the vomiting for a further week, when she was admitted to another hospital and treated with gastric lavage and a fluid diet. The vomiting ceased after three days on this regime. She was transferred to Addenbrooke's Hospital on December 22, 1949, when she gave the above history. She had had no other serious illnesses in the past. Her husband and two children were alive and well and there was no family history of diarrhoea or abdominal illness.

She was a thin, white-haired woman. Her tongue was smooth, and red at the tip and round the sides, but was otherwise normal. Her abdominal wall was very thin and

Radiograph after barium meal, showing multiple duodenal and jejunal diverticula, and a large diverticulum on the duodeno-jejunal flexure.

intestinal peristalsis could be seen. There were no other abnormal physical signs. On December 28 barium meal examination showed multiple duodenal and jejunal diverticula and a large diverticulum on the duodeno-jejunal flexure (see Fig.). Diverticula contained fluid levels in the erect position. Barium flocculated in the jejunum and ileum. Transit time slow, 7½ hours. The calibre of the small gut was wide (Dr. F. R. Berridge). Blood count (see Table) showed a slight macrocytic anaemia.

On January 2, 1950, the serum calcium was 11.1 mg. per 100 ml.; serum phosphorus, 2.8 mg. per 100 ml.; plasma protein, 5.6 g.% (albumin 2.6 g., globulin 3 g.); non-protein nitrogen, 53 mg. per 100 ml.; thymol turbidity, 3 Maclagan units; thymol flocculation, negative. *X*-ray film of forearm bone with control—no significant abnormality. An amino-acid absorption test was normal. A sternal puncture on January 14 showed: total cell count, 20,000 per c.mm.—megakaryocytes 6 per 10,000 nucleated red cells, M/E ratio 3.2:1; polymorphs—neut. 36.5, eos. 2.6; metamyelocytes—neut. 15.6, eos. 1.8; myelocytes—neut. 9.4, eos. 0.6; premyelocytes, 2.4; myeloblasts, 0.2; lymphocytes, 9.4; plasma cells, 0.2; monocytes, 0.6; normoblasts—late 12.6, intermediate 2.0, early 0.6; megaloblasts—late 4.0, intermediate 1.0, early 0.8; pre-erythroblasts, 0.4; haemocytoblasts, 0.2; megaloblasts of nutritional macrocytic anaemia type (Dr. Martin Hynes). On January 17 a glucose-tolerance test showed: fasting, 0.095%; 30 minutes, 0.176%; 60 minutes, 0.204%; 90 minutes, 0.148%; 120 minutes, 0.132%. A fat balance was unfortunately not completed successfully, and the patient did not wish further investigation.

She was discharged home on a low-fat (50 g.) high-protein diet, ascorbic acid, vitamin B_1, nicotinic acid, and riboflavine; and also folic acid, 10 mg. t.d.s., which was begun on January 17. The reticulocytes on January 20 were only 0.5%, and on the 27th they were 1.8%. She continued with folic acid, 5 mg. b.d., and on February 3 a blood count showed no improvement. By March 17 the red-cell count had risen, and the macrocytosis was less, but the diarrhoea had persisted, and the tongue was still sore, with a smoother appearance than previously. In April, 1950, the folic acid was discontinued for one month, with no change in symptoms. The vitamins were discontinued in

May, and folic acid, 5 mg. b.d., was started again. Symptoms remained unchanged, with the tongue sore most of the time, but the patient felt better in herself. By July 14 the blood count had returned to normal and the macrocytosis had disappeared. She continued with folic acid, and in spite of this in September a blood count showed a fall in the red cells and a return of macrocytosis. Her serum calcium was 9 mg. per 100 ml., plasma proteins 5.8 g.% (albumin 3.6 g., globulin 2.2 g.). The patient complained of feeling generally tired and unwell, and agreed to come back into hospital, which she did on November 27.

A fat balance investigation was carried out, the balance period being four days on a standard 50-g. fat intake, and the result was as follows: dry matter, 6.4% of faeces; total fat, 28.2% of dry matter; neutral fat, 0.8%; free fatty acid, 26.2%; soap fatty acid, 1.2%; fat hydrolysed—93% of total fat. Fat intake was 202 g. over four days, and fat lost 31 g.=15.3% of fat intake. Fasting gastric juice free HCl 0.045%, total 0.073%. After histamine, free HCl 0.273%, total acidity 0.310%. Duodenal juice showed some lipase and tryptic activity, but no quantitative test was attempted. The patient complained of a sore tongue, and it was moderately smooth and reddened. She was treated with two injections of riboflavine, 10 mg., vitamin B_1, 50 mg., nicotinic acid, 50 mg., followed by a further six injections at twice-weekly intervals. Her tongue became extremely sore, and was dark red and beefy in appearance, with complete loss of papillae. She was discharged home, and her tongue remained sore.

In December, 1950, she was started on injections of crude liver extract ("plexan"), 4 ml. twice weekly. Within 14 days the soreness of her tongue disappeared and in a month it looked virtually normal. She continued on injections of plexan, 4 ml., which after a month were changed to weekly, and then to fortnightly after a further two months, until July, 1953. During this time her blood count remained very satisfactory, being normochromic and normocytic. She did, however, continue to have looseness of her bowels with three or four stools a day, and occasionally more severe diarrhoea. At intervals she experienced abdominal discomfort, vague indigestion, and occasional attacks of vomiting lasting a day or two. In May, 1953, she developed more frequent indigestion with vomiting every few days for a period of about a month.

On June 4 she was started on a course of chlortetracycline, 250 mg. six-hourly, which she continued for nine days, receiving 9.25 g. in all. The injections of plexan were discontinued in July. Following the chlortetracycline her stools became more normal over the course of a fortnight, and since July, 1953, she has had two, or occasionally three, normally formed motions each day for the first time for several years. Unfortunately the patient was unwilling to be admitted for a further fat balance investigation. This improvement in her bowels continued until March, 1954. During this period of eight months she had had only three or four slight vomiting attacks. She had no recurrence of soreness of the tongue, and her blood count, carried out at monthly or two-monthly intervals, remained normal. She is a patient who has always complained very readily in the past, but she said that she had felt better since she had the course of chlortetracycline than she had done for years.

This satisfactory state of affairs ceased at the end of March, 1954, when she began to have more frequent attacks of vomiting and developed a sore smooth tongue again. She was started again on weekly injections of plexan, 4 ml., on April 23, and these were continued for three weeks. On April 26 an analysis of one specimen of stools showed that 37.6% of the dry matter was fat. On April 30 she was started on a week's course of chlortetracycline, 250 mg. six-hourly, totalling 7 g. Following this she continued to feel unwell for two weeks, but then began to improve again. Her sore tongue had begun to improve before this, and by May 28 was normal. At the time of writing she appears to be well.

Discussion

It is of interest that although the anaemia responded to refined liver extract and to folic acid, the glossitis showed no improvement. Treatment with crude liver extract, however, resulted in disappearance of the glossitis within a fortnight, and improvement in the patient's feeling of well-being. There was no change in the diarrhoea. Following the course of chlortetracycline her stools became formed for the first time for several years, and she felt better than she had done for a similar period. The anaemia and glossitis also remained in remission without further injections of crude liver extract after the course of chlortetracycline, but this may have been the result of the necessary factors having been stored from the large quantities of crude liver she had received during the previous two years. It does appear, however, that the chlortetracycline exerted some effect on her intestinal function.

Of the various possible mechanisms whereby small-intestinal dysfunction, with impairment of absorption, may be provoked, the presence of infection inside the small bowel is one which has been put forward as responsible in several distinct pathological conditions. Cameron, Watson, and Witts (1949), in experiments on rats, showed that transection of the small gut followed by end-to-side anastomosis, in such a way as to produce a small blind loop which emptied itself downwards, was not followed by anaemia unless there was some stenosis of the opening of the blind loop causing stagnation. If, however, the blind loop was made at the end of the proximal piece of gut, so that stagnation occurred in it, a percentage of the rats so treated developed a macrocytic anaemia. These authors noted that it was important to place the blind loop in the upper or middle part of the small intestine. When the loop was in the lower ileum very few rats developed anaemia. It seems very probable that the steatorrhoea associated with gastro-colic fistula is due to soiling of the small-intestinal contents by material from the large bowel. It has been suggested that the steatorrhoea which sometimes develops after a Polya type of gastrectomy, and which may appear many months after the operation, is the result of stagnation in the afferent loop, with subsequent infection.

The state of affairs existing in multiple jejunal diverticulosis is clearly one in which stagnation and infection in the sacs might be expected to occur. To prove that infection is present in the diverticula is an extremely difficult matter except by the method of direct sampling should the patient require a laparotomy. Taking samples through a Miller–Abbott tube introduces too many possibilities of contamination. In this patient the reversion of the bowel habit to normal after a course of chlortetracycline does suggest that the removal of infection might have been one factor responsible, and it does seem possible that infection in the diverticula may have been in part responsible for the small-intestinal dysfunction.

Summary

A case of jejunal diverticulosis, complicated by steatorrhoea, macrocytic anaemia, and glossitis, is described.

Parenteral crude liver extract produced a complete remission of the glossitis and macrocytosis. Parenteral refined liver extract, oral folic acid, and massive vitamin B therapy had no effect on the glossitis, while the macrocytosis showed a variable response to refined liver extract and folic acid.

Improvement in the diarrhoea and in general health occurred after a course of chlortetracycline, and the glossitis and anaemia remained in remission, without further treatment with crude liver extract, for a period of eight months.

It is suggested that the multiple jejunal diverticulosis was responsible for the steatorrhoea in this case, and

that stagnation and infection in the diverticula may have been the most important factor in producing the small-intestinal dysfunction.

REFERENCES

Benson, R. E., Dixon, C. F., and Waugh, J. M. (1943). *Ann. Surg.*, **118**, 377.
Braithwaite, L. R. (1923). *Brit. J. Surg.*, **11**, 184.
Butler, R. W. (1933). Ibid., **21**, 329.
—— (1937). Ibid., **25**, 277.
Cameron, D. G., Watson, G. M., and Witts, L. J. (1949). *Blood*, **4**, 803.
Edwards H. C. (1939). *Diverticula and Diverticulitis of the Intestine*. Wright, Bristol.
Montuschi, E. (1949). *Proc. roy. Soc. Med.*, **42**, 868.
Phillips, J. H. C. (1953). *Brit. J. Surg.*, **40**, 350.
Stiven, H. E. S. (1934). *Lancet*, **2**, 704.
Waterson, A. P. (1952). Ibid., **2**, 1053.

ANTIBIOTIC SENSITIVITY SPECTRA

THEIR USE IN INVESTIGATING EPIDEMICS

BY

E. P. SILBERSTEIN, M.B., B.S., B.Sc.

Formerly Senior House Officer to the Pathologist, Ashford Hospital, Middlesex

Staphylococcal infections in hospital wards are the cause of considerable morbidity and mortality, and for many years bacteriologists have been devising methods to facilitate the detection of sources of infection. One of the difficulties has always been the fact that coagulase-positive staphylococci are commonly found in the upper respiratory tract and skin of apparently healthy people, and it is not practicable to eliminate all of these. "Unless the epidemic strain has some special characteristic, it is impossible to decide whether, for instance, a carrier of the species concerned is to be incriminated. It is here that the definition of individual 'types' within species has been found so valuable" (*Lancet*, 1947). Serological typing and phage-typing were used by Allison and Hobbs (1947) in their brilliant investigation of neonatal infections. Phage-typing has indeed been a new and successful weapon in tracing the sources of wound infections, but it requires some experience, and it is not used by many routine laboratories. When we were faced with investigation of an epidemic of wound infections in our surgical wards it was thought that antibiotic sensitivity patterns might help to determine the cause of the trouble.

Investigation

Between September 12 and 24, 1953, five patients developed wound abscesses seven to ten days after an elective operation. The pus from the wounds yielded pure cultures of *Staphylococcus pyogenes*, and these infections appeared to be confined to patients operated on by one surgical team.

Nose and throat swabs were taken from all the nursing staff in the theatre and wards (22 in all), from the anaesthetist, and from two members of the surgical team. (The third member of the surgical team was away for three weeks when this investigation was started, but he had been present at all the operations done on the cases that became infected.) Coagulase-positive staphylococci were found in over half of the nursing staff. It was thus most desirable to determine whether all these staphylococci belonged to the same strain. Sensitivities to penicillin, streptomycin, chloramphenicol, chlortetracycline ("aureomycin"), and oxytetracycline ("terramycin") were determined with standard pads of these antibiotics on blood-agar plates, and three different patterns were obtained from the nursing staff (see Table I). Although the organisms derived from the wounds all gave the same pattern (Table II), this did not coincide with any of the patterns derived from the nursing staff. The pattern, however, did coincide with that derived from organisms obtained from the nose and conjunctivae of

TABLE I.—*A, B, and C are Antibiotic Sensitivity Patterns of Strains of Staph. pyogenes Obtained from the Nursing Staff. All Coagulase-positive Staphylococci Derived from Them Belonged to One of these Three Strains*

Antibiotic	A	B	C
Penicillin	++	−	−
Streptomycin	+	+	−
Chloramphenicol ..	+	+	+
Aureomycin	+	+	−
Terramycin	+	+	−

++=Very sensitive, +=sensitive, −=resistant.

TABLE II.—*Sensitivity Spectra of Strains of Staph. pyogenes Obtained from the Pus of the Patients (D), and the Nose and Conjunctivae (E and F Respectively) of the Missing Member of the Surgical Team*

Antibiotic	D	E	F
Penicillin	−	−	−
Streptomycin	−	−	−
Chloramphenicol ..	−	−	−
Aureomycin	+	+	+
Terramycin	+	+	+

+=Sensitive; −=resistant.

the missing member of the surgical team (Table II), who had just returned from his holiday at this stage of the investigation. (While on holiday he had suffered from acute blepharitis and conjunctivitis.) Intensive antibiotic therapy was given and his infection was eradicated. There have been no further staphylococcal wound infections in the wards of his surgical team. It should be added that none of the patients operated on while he was on holiday developed staphylococcal wound infections.

Discussion

The value of *in vitro* sensitivity tests in the treatment of infections is still a somewhat controversial subject. The same can be said of our views on the action of antibiotics in their role as antibacterials. The most widely accepted and most plausible theory seems to be the one which ascribes to the antibiotics a power of interfering with some enzyme system which is essential either for bacterial survival or for their multiplication. Where a species of micro-organism displays great variations in sensitivity to an antibiotic, such as, for instance, *Staph. pyogenes*, the organisms that are sensitive would rely for survival or multiplication on some enzyme system which is interfered with by the antibiotic —for example, by poisoning, competition, or blocking—and the ones that are resistant either do not require this enzyme system or have developed an alternative one. It would seem to be a reasonable assumption that a variant strain of one species relies in its metabolism on the same or similar enzyme systems. Antibiotic sensitivity patterns may therefore be useful in tracing strains of bacteria and in finding sources of infection. The determination of antibiotic sensitivity spectra is a simple procedure that can be carried out in routine bacteriological laboratories, and if it can be relied upon to separate different strains of a species of micro-organism this should provide a useful screening test for sources of infection.

The absence of further wound infections after eliminating virulent organisms from the eyes and respiratory tract of a member of the surgical team is, it is felt, strong evidence that he indeed was the source of infection, as is the fact that none of the patients operated on during his absence developed staphylococcal wound abscesses. Antibiotic sensitivity patterns suggested that the staphylococci in the wounds and in his nose were the same strains, and thus showed us where to find the cause of our trouble and how to deal with it.

Phage-typing was carried out on some of the cultured strains by the Staphylococcal Reference Laboratory, Colindale. This showed that staphylococci with different sensitivity patterns were of different phage types and that those with the same patterns were of the same phage types (Table III). That there is a close analogy between phage

TABLE III.—*Phage Patterns of Staphylococci Obtained from the Nursing Staff (A, B, C), the Infected Wounds (D), and the Surgeon (E and F)*

Phage Patterns	A	B	C	D	E	F
Diluted .. Undiluted ..	52A v.w. 52/52A/79	— 73+	— 29+	75+W	75+W	75+W

type and antibiotic sensitivity is also suggested by investigations on penicillin-resistant strains and their phage types (Selbie, 1953). In the case of erythromycin- and carbomycin-resistant staphylococci there would appear to be no correlation between antibiotic resistance and phage type (Hobson, 1954), although the author does not state whether the phage type was checked after the development of antibiotic resistance.

Sensitivity spectra, using penicillin, streptomycin, chloramphenicol, and the tetracyclines, certainly seem to be of use in the determination of strains of staphylococci, and they were of considerable value in rapidly tracing the source of wound infection in this instance.

I wish to thank Mr. Weait and Mr. Oke, who did most of the technical work and played a vital part in this investigation, Mr. D. Morris and his surgical team for asking for this investigation to be carried out and for supplying the specimens of pus, and Dr. W. F. Hamilton for permission to publish. Dr. R. E. O. Williams of the Streptococcus and Staphylococcus Reference Laboratories very kindly did the phage-typing.

REFERENCES

Allison, V. D., and Hobbs, Betty C. (1947). *British Medical Journal*, 2, 1.
Hobson, D. (1954). *Lancet*, 1, 236.
Lancet, 1947, 2, 19.
Selbie, F. R. (1953). *Practitioner*, 171, 239.

Medical Memoranda

Two Cases of Favism in Israel

Favism is an acute febrile haemolytic anaemia caused by an unknown factor present in *Vicia fava*, the broad-bean. The disease is contracted by ingestion of the fruit, leaves, roots, stem, or flowers of this plant. It has been said that even the pollen can give rise to the condition. The toxic factor is resistant to weather and heat, and is transmitted via the milk of both the cow and the nursing mother.

No age is exempt, but favism occurs chiefly in children, and males are affected more than females. Some hereditary factor may be present, as the condition has been seen in Israel only among the Oriental population—the Sephardic and Yemenite Jews and the Arabs. So far no authentic case has been reported in the European or Ashkenazi communities. There is a definite seasonal incidence. Most of the cases occur in spring, during February, March, and April, when the broad-bean blossoms. Favism has an affinity with two other haemolytic anaemias—namely, Bagdad spring anaemia and the acute febrile haemolytic anaemia of Lederer. The former, an acute haemolytic anaemia, occurs in Bagdad during a few weeks in the spring, and is said to be due to an allergic reaction to contact with flowers (*Verbena hybrida*) and young fruits. Lederer's anaemia, which gives rise to a similar clinical picture, is said to be due to an allergic response to the streptococcus, the pneumococcus, or the dysentery bacillus. It occurs chiefly in children. The following two cases of favism occurred in Beerva, a Yemenite village situated some nine kilometres from Acre in Western Galilee, Israel.

CASE 1

A boy aged 12 suddenly fell ill on the night of April 17, 1952. At 7 p.m., after supper, he felt sick and vomited twice. Up to that time he had been perfectly well. A little later he passed a small amount of "bloody" urine and felt very faint; at about 9.30 p.m. he had a fit (probably due to acute central anoxia). Some relatives obtained transport and called me, and I reached his bedside at 10.15 p.m. The boy was shocked, very pale, and semicomatose. Ocular and tendon reflexes were present and brisk, but there was no plantar response. The limbs were twitching spasmodically. There was no neck rigidity. He was sweating profusely and the extremities were cold. The pulse was small and thready, with a rate of 140 a minute, and the tongue dry and coated. There were no abnormal signs in the chest. The liver was palpable two fingerbreadths below the costal margin, but the spleen could not be felt. Rectal temperature was 100.4° F. (38° C.). The urine was of a deep port-wine hue, and almost opaque against the light. There was no history of malaria or intake of any drugs. The only positive fact in the history was that the patient, like everyone else in the village, had been eating broad-beans for the past two weeks.

After receiving 2 ml. of nikethamide intramuscularly, the patient was taken to the Haifa Government Hospital, arriving there 45 minutes later. His haemoglobin was found to be 3 g. per 100 ml. (Sahli). He was transfused immediately with 500 ml. of bank blood, and the next morning his haemoglobin had risen to 5 g. per 100 ml. A further 750 ml. of blood was given, and the haemoglobin rose to 7 g. per 100 ml. and the erythrocyte count to 2,360,000 per c.mm. The results of other investigations were:—Urine: acid, albumin +++, haemoglobin +++, and crystals of haemin +++ in the deposit. W.B.C., 22,000 per c.mm. (polymorphs 80%); serum bilirubin, 10 mg. per 100 ml.; thymol turbidity and Takata–Ara, negative; Weltmann, 8 units; plasma proteins, 7.6 g. per 100 ml. (albumin/globulin ratio 1.81:1); blood urea, 100 mg. per 100 ml.; blood cholesterol, 125 mg. per 100 ml. Mantoux, negative at 1:1,000.

Recovery was uneventful and the patient was sent home after eight days, on continued treatment with ferrum redactum 3 g. daily and a full diet.

CASE 2

This boy, also aged 12, became ill 10 hours after Case 1. If anything, his condition was even worse. His haemoglobin level was 3.5 g. per 100 ml. when he left for the hospital, but by the time he reached Haifa (within one hour) it had fallen to 2 g. per 100 ml. Ultimately he also recovered after two blood transfusions, and was discharged home after two weeks. Likewise in his history there was nothing relevant, except that he also had been eating broad-beans.

COMMENT

No other case of favism occurred in the village during the year (1952). Once the condition had been recognized the villagers were warned neither to eat broad-beans nor to bring them into their homes, and particularly to keep their children away from them. One does not know how far this affected the incidence of the disease, as up to then they all had been eating the bean, cooked as well as uncooked. But the fact remains that none of the other 150 children developed the disease.

Favism has been confounded with divers conditions such as food-poisoning, acute haemorrhagic nephritis with uraemia, blackwater fever, drug haemolysis, and pneumonia. Toxic haemoglobinuria due to drugs such as quinine, the sulphonamides, potassium chlorate, nitrites, pyridine, the aniline drugs, etc., also enters into the differential diagnosis. Particularly in Israel, especially in the malarious districts of upper and eastern Galilee, one must rule out the possibility of blackwater fever. Acute infections such as typhus,

septicaemia, meningitis, pneumococcal infections, etc., may at times be associated with toxic haemoglobinuria as a result of an acute haemolytic crisis.

One is struck by the dramatic onset of favism: it can result in the destruction of more than 75% of the red cells in the blood within 24 hours. However, the response to blood transfusion is nothing short of miraculous. Favism can recur, and the only prevention is to refrain from eating the broad-bean.

S. MANSOOR, M.D.
Acre, Israel.

Treatment of Rheumatoid Arthritis with Organic Copper Compounds

Improvement in cases of rheumatoid arthritis treated with an organic compound of copper was reported by Forestier and Certonciny (1946), who referred to the previous work of Fenz (1941) in Germany.

The drug, cuproallyl-thiourea-sodium benzoate, is a yellowish-brown crystalline powder containing 19% of copper and readily soluble in water. The solution is irritating to the tissues and must be administered intravenously. It accumulates in the liver and to a lesser extent in the spleen, kidneys, lungs, heart, and brain. Excretion is mainly by the intestine and is slow, continuing after administration has ceased.

Forestier and Certonciny, following the German workers, at first used small doses of 0.01 to 0.1 g., averaging 1 g. for a course. Finding that the drug was well tolerated, they increased the dose, giving 0.25 to 0.5 g. twice weekly, administering up to 5 g. in a course. Doses were given intravenously, dissolved in 10 ml. of sterile distilled water. Courses of treatment were repeated at the end of a month and again at intervals of two or three months. No toxic effects were encountered.

Results were better with the higher dosage. Out of a series of 40 cases improvement was noted in 80%, the result being excellent in 15%. But most of the good results were in early cases of less than one year's duration.

A trial by Tyson *et al.* (1950) in a series of 20 cases was not encouraging. Kuzell *et al.* (1951), in a group of 31 patients, failed to confirm the claims made for the drug: at the best they thought there might be a slight therapeutic effect in cases associated with psoriasis.

Through the courtesy of Lumière a small quantity of the preparation was obtained and tried in a few cases with indefinite results.

May & Baker Ltd. then synthesized two compounds: "alcuprin" (sodium *m*-(N-allylcuprothiocarbamide) benzoate) for intravenous use, and "cuprimyl" (a copper complex of 8-hydroxyquinoline bis-(diethylamine sulphonate)) for intramuscular injection. A trial was begun with these on a group of well-established cases of rheumatoid arthritis, in four of which chrysotherapy had been given. For descriptive purposes the cases are graded as follows: grade 1, physical signs slight; grade 2, well-marked physical signs but general condition good; grade 3, extensive physical signs with wasting and poor general condition; grade 4, extensive physical signs with poor general condition, wasting, and crippling.

Case No.	Sex	Age	Duration of Illness	Grade	Sedimentation Rate		Result
					Before	After	
1	M	24	3 years	1	6	3	Slightly improved
2	M	41	6 "	1	8	5	"
3	M	62	5 "	1	5	12	Unchanged
4	F	35	3 "	2	22	21	"
5	F	57	10 "	2	20	25	"
6	M	43	5 "	3	18	9	"
7	F	45	3 "	3	37	38	"
8	M	52	13 "	3	25	25	"
9	F	65	3 "	3	27	75	Worse
10	M	45	2 "	4	87	100	Unchanged

All patients had two courses of treatment, each course comprising 10 doses of 0.25 g. of alcuprin with a total of 2.5 g., or 0.5 g. of cuprimyl with a total of 5 g. Patients were under observation for three months before treatment and one year after. Toxic effects were not observed. The results are set out in the Table.

No therapeutic effect was demonstrated in the group. The trial was an exacting one on a selected group from which early cases had been excluded, and in consequence a sustained improvement could with confidence have been attributed to the drug. Early cases were excluded because the fluctuating course of some and the occasional occurrence of spontaneous remissions make assessment difficult; also the early stage of the disease may be modified by a number of drugs which have no lasting effect. Though a further trial in this early type of case seems worth while, assessment is difficult.

Two patients (Cases 3 and 5) had psoriasis, which was not influenced by the drug.

I am indebted to May & Baker Ltd. for ample supplies of both drugs for this trial.

T. J. O'REILLY, M.D.,
Dublin Rheumatism Clinic.

REFERENCES

Fenz, E. (1941). *Münch. med. Wschr.*, **88**, 1101.
Forestier, J., and Certonciny, A. (1946). *Presse méd.*, **54**, 884.
Kuzell, W. C., Schaffarzick, R. W., Mankle, E. A., and Gardner, G. M. (1951). *Ann. Rev. Med.*, **2**, 390.
Tyson, T. L., Holmes, H. H., and Ragen, C. (1950). *Amer. J. med. Sci.*, **220**, 418.

Fat Embolism in Thoracic Operations

Fat embolism as a complication of operative procedures has been described in association with orthopaedic and abdominal surgery, but little reference has been made to its possible occurrence in thoracic operations. In view of the growing importance of cardiac surgery it is felt that the following observations are worthy of record.

Over the past two years small fragments of lung tissue from patients subjected to mitral valvotomy have been submitted for routine histological examination. During study of these biopsy specimens in two cases the large and medium-sized pulmonary arteries were found to contain bone marrow. Frozen sections stained by Scharlach R were employed on all subsequent lung biopsies from valvotomy patients, and in 4 out of 24 a minor degree of fat embolism was noted. Similar studies were made on pneumonectomy and lobectomy specimens. In one case bone marrow was present in the major pulmonary arteries, and in 10 out of 17 cases a slight degree of fat embolism was noted in frozen sections.

The occurrence of fat embolism in valvotomy patients is not altogether surprising, since the operative procedure entails continuous rib retraction and considerable trauma is possible. Fractures have even been recorded in some cases. The actual severance of ribs during pneumonectomy and other thoracic operations accounts for the higher incidence of fat embolism in this group. Vance (1931) has suggested that a slight degree of fat embolism cannot always be regarded as confirmatory evidence of trauma, since he found it in a small percentage of cases of non-traumatic deaths, but the presence of bone marrow in three cases in this series indicates a definite relationship to surgical trauma.

Whilst it is extremely unlikely that the degree of fat embolism evoked by such operative procedures as mitral valvotomy might assume clinical significance, it should, however, be borne in mind that it can occur, and even to such an extent that bone marrow is discharged into the pulmonary vessels.

FLORENCE MCKEOWN, M.D.
Institute of Pathology, Belfast.

REFERENCE

Vance, B. M. (1931). *Arch. Surg. (Chicago)*, **23**, 426.

Reviews

THE STORY OF GUY'S

Mr. Guy's Hospital, 1726–1948. By H. C. Cameron, M.D., F.R.C.P. (Pp. 520+xiii; illustrated. 30s.) London, New York, Toronto: Longmans, Green and Co. 1954.

It is over sixty years since there appeared the interesting *Biographical History of Guy's Hospital* by Wilks and Bettany. During this time much has happened, and with the great changes incidental to the introduction of the new health service there was need for a complete history of this famous institution. Dr. Cameron, for many years a distinguished member of the medical staff of Guy's, has undertaken this difficult and arduous task and achieved a remarkable success. It is indeed a notable feat to have compressed within 500 pages the story not only of the hospital itself but of the medical, dental, and nursing schools, not to mention short biographical sketches of about sixty of the past members of the staff. The book is well illustrated, and there are four beautiful coloured plates. We would warn the reader that many of the 174 footnotes in small print are of great interest and should not be missed.

It is impossible to do justice to this book within the limits of a short review, but some outstanding impressions remain. In the early part the figure of the famous treasurer, Benjamin Harrison junior, stands out boldly, the perfect picture of the absolute autocrat. He created the medical school and controlled it so efficiently and fully as to illustrate aptly the view that the best form of government is a wise and benevolent autocracy. In later years, when the superintendent shared with the treasurer the weight of administration, Cooper Perry was most influential. The tradition of complete independence and self-sufficiency, very satisfactory in the earlier years, later became a drag on the wheels and appears to have been responsible for the late adoption of some methods which had already proved their worth elsewhere. One reads with amazement of the bitter dispute between the medical staff and the governors over the introduction of the nursing reforms of 1880.

Dr. Cameron's deep knowledge of the history of the Society of Apothecaries enables him to throw much light on the growth of the medical curriculum; indeed, he gives a better outline of the history of medical education in this country during the past century than can be found anywhere else.

In the short biographies of past members of the medical staff one finds many pen-pictures which remain in the memory: Addison denouncing the system of scholarships and prizes because he thought they encouraged the student to concentrate too much on one subject; Bright demonstrating albuminuria by heating a little urine in a teaspoon with the aid of a candle; Cooper Perry, looking the picture of misery in the lecture room, sitting down with his head between his hands and his eyes glued to his manuscript; Herbert French writing his famous *Index* while he was being whirled along in a car to a distant consultation; the kindly and hard-worked Rowlands speaking fluently in English but always thinking in Welsh; the earnest young Ryle taking the names and addresses of out-patients whom he later visited with a view to helping them out of difficulties—these and many other pictures delight the reader.

We should think that every good Guy's man will want to have this book on his shelves, and we are sure that everyone interested in the history of medicine or medical education will need to refer to it.

ZACHARY COPE.

HUMAN PHYLOGENY

Man's Ancestry: A Primer of Human Phylogeny. By W. C. Osman Hill, M.D., F.R.S.Ed. (Pp. 194; illustrated. 21s.) London: William Heinemann Medical Books Ltd. 1954.

Dr. Osman Hill's book had its origin in a course of lectures given at Edinburgh University to a group of students, mostly of social anthropology, some of whom had no previous biological training. His aim has been to provide a short textbook for students of human affairs who need to understand something of man's evolutionary origins, and in doing this to cater also for the intelligent layman. In general he has succeeded admirably, although the book, being set out in the systematic fashion appropriate to a student's text, may seem rather heavy going to the layman whose interest is not very determined.

Dr. Hill paints on a broad canvas. The first chapter summarizes the general evidence for evolution, the emphasis being on a rather old-fashioned approach which tends to neglect the more recent genetical work. There follows a summary of the phylogeny of invertebrates and then of chordates as deduced from comparative anatomy. We then pass on to an outline of the evolution of the nervous system, and thus to the rise of the primates. This is illustrated by clear diagrams of the various tracts in the brain as they appear to the morphologist. These have considerable heuristic value, but the caution in their interpretation suggested by recent physiological analysis might have been more stressed.

Finally we come to the core of the book—four chapters devoted to the anthropoids and the emergence of man. This contains an adequate and systematic survey of the fossil evidence, and most of the current theories concerning this controversial field are briefly mentioned. Dr. Hill's own views tend to be conservative; he considers the South African Australopithecinae to be much nearer apes than man, and he seems unwilling to accept fully the recent work which suggests that Piltdown man was a fake. In his final section also, on the evolutionary mechanisms which brought about the rise of man, little attention is paid to the recent developments of evolutionary genetics. Nevertheless Dr. Hill's book will undoubtedly be very useful as a text for students who are making their first acquaintance with this complex subject.

C. H. WADDINGTON.

PERIPHERAL CIRCULATION

Peripheral Circulation in Man: A Ciba Foundation Symposium. Edited for the Ciba Foundation by G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch., and Jessie S. Freeman, M.B., B.S., D.P.H., assisted by Joan Etherington. (Pp. 219; 72 illustrations. 25s.) London: J. & A. Churchill Ltd. 1954.

This book contains not only the papers read at a recent meeting sponsored by the Ciba Foundation, but also a full account of the discussions that followed. These add greatly to its value and reproduce some of the give and take of a successful scientific meeting. It provides a stimulating account of progress in an important field of vascular physiology, and is complementary to a previous similar volume on visceral circulation.

All the articles reach a high standard. Burton contributes an admirable critical survey of methods available for the measurement of peripheral blood flow which could be read with advantage by anyone interested in general physiology. A new and versatile method of detecting and measuring changes in blood flow by the electrical strain gauge is described by Whitney. Those to whom it appeals would be well advised to read the discussion of this paper, which brings out clearly its merits and defects. Von Euler gives an authoritative account of the capacity of the suprarenal glands to produce either adrenaline or noradrenaline to meet the homoeostatic requirements of the body. Whelan describes the effects of these substances on the blood flow through human skeletal muscle in a short paper which led, however, to the longest and perhaps most illuminating discussion in the book.

Various aspects of blood-flow responses to alterations in temperature are dealt with by Carlson, by Greenfield, and by Barcroft and Dornhorst. The last two authors put forward the unusual view that there are in muscle two functionally independent circulations—one subserving metabolism and controlled by local conditions, and another concerned with circulatory homoeostasis subserved by the sympathetic nerves and certain hormones. Papers with a more direct bearing

on clinical problems are provided by Dible in a thoughtful article on peripheral ischaemia in man, and by Guttmann on the circulation in spinal man. Martin outlines the methods of investigation he has found most helpful in surgical practice.

The book is highly recommended to all those who are interested in circulatory problems.

E. J. WAYNE.

EXPERIMENTAL ALLERGY

Experimental Allergic Reactions Induced by Simple Chemical Compounds. By Mitsuteru Ishikawa, M.S., M.D. (Pp. 122; $2.00.) Tokyo: Maruzen Company, Ltd. 1953.

This is an account of a series of studies of the inducement of hypersensitivity to simple chemical compounds. The compounds include arsenious acid, aspirin, salicylates, picric acid, and formaldehyde. Hypersensitiveness was induced by intracutaneous injection; better results were obtained if the compounds were mixed with horse serum or with other adjuvants, including gum arabic and agar. The hypersensitivity was manifested by mild delayed skin reactions rising to a maximum in 20 to 24 hours after the inducing compound had been injected into the skin; all that is said about the histology is that the characteristic changes were swelling of the fibrous tissue and diffuse hyperaemia of varying degrees. Hypersensitivity could be transferred to normal skin by injection of serum of a sensitized animal; this is unusual in this type of hypersensitivity. As all but two of the 168 papers quoted are in Japanese and some of the results are rather unexpected, it is a pity that some of the experiments are not described in fuller detail. Neither Landsteiner nor Chase is mentioned in the discussion.

J. R. MARRACK.

RADIODIAGNOSIS OF THE CERVICAL SPINE

Funktionelle Rontgendiagnostik der Halswirbelsaule. By Dr. C. Buetti-Bauml. (Pp 160+viii; illustrated. D.M.42.) Stuttgart: Georg Thieme. 1954.

This monograph on functional radiodiagnosis of the cervical spine was awarded its Jubilee Prize by the Swiss Röntgen Society. It is a brilliant and thorough discussion of a difficult and important subject and will well repay careful study. It is fully illustrated by 154 radiographs, taken with great skill and ingenuity and superbly reproduced full-scale. They show normal and abnormal conditions of the cervical spine in various positions, each taken in such a way as to bring out clearly the precise details required. Each is accompanied by a short account of the case and frequently by an explanatory diagram.

It is indeed a remarkable volume, founded on wide experience, infinite patience, and quite exceptional ingenuity. The descriptions are brief and accurate, and with the accompanying radiographs give a clear view of each case. We could not imagine any account of greater value to those who wish to study the complex and difficult conditions which may arise in this region of human anatomy.

HENRY SOUTTAR.

CHILD CARE

Babies and Young Children: Feeding, Management, and Care. By Ronald S. Illingworth, M.D., F.R.C.P., D.C.H., and Cynthia M. Illingworth, M.B., B.S., M.R.C.P. (Pp. 360 +vii; illustrated. 18s.) London: J. and A. Churchill Ltd. 1954.

A new book called *Babies and Young Children* by Professor R. S. Illingworth and his wife should really be reviewed by the mother of a family. The authors make it clear that they are writing for parents and not for doctors, and it is in this light that it must be judged. In general they appear to have succeeded well in imparting information in an easily understood style, although here and there a bit of jargon creeps in. A description of some phenomena as of no significance may be quite plain to the medical mind, but for the lay parent it would perhaps have been better to say that it was "nothing to worry about." Again, it is of doubtful value to say much about common ailments in a book which is primarily intended to preach health and prevention. However, perhaps the intelligent mother will like these sections. The reviewer was especially pleased with the sections dealing with the psychological aspects of child development. Two chapters headed "On Love and Security" and "Discipline" especially go to the root of the matter.

Clearly Professor and Mrs. Illingworth have learnt much from their own family, and this gives a personal touch to the book. The drawings and photographs are well chosen. Family doctors should have no hesitation in recommending this book to parents. Despite the authors' declared intention, most doctors, including paediatricians, will also learn from it.

ALAN MONCRIEFF.

RADIOLOGY OF THE DIGESTIVE TRACT

The Digestive Tract in Roentgenology. Volumes I and II. By Jacob Buckstein, M.D. Second edition. (Pp. 1202 the two volumes; illustrated. £12.) Philadelphia, London, and Montreal: J. B. Lippincott Company. 1953.

The second edition of this work runs into two volumes with over 1,500 illustrations—half as many again as the single-volume edition of 1948. A very large amount of clinical material is discussed in the illustrative cases described under different disease entities, all being beautifully illustrated. Discussion in all sections is clear and precise, and adequate bibliographies are included. Many useful clinical as well as radiological comments are made by the author, and for this reason alone the book deserves the attention of all interested in the subject. Though rare diseases are discussed in detail, balance has not been lost, and important subjects like the radiological diagnosis of malignant ulceration of the stomach receive merited treatment. The section dealing with small-bowel conditions is most valuable, and the radiologist faced by the occasional neonatal small-bowel obstruction or mesenteric tumour will find them dealt with comprehensively. In any publication of this size omissions are almost inevitable, and when dealing with ulcerative colitis the author makes no mention of the possibility of carcinoma of the colon developing as a late feature in the chronic case in which clinical cure appears to have been achieved. Again, in the section on diverticulitis of the colon the differential diagnosis of diverticulitis and carcinoma is not discussed, though the fact that one may simulate the other is referred to. Yet these are only minor faults in an excellent book, of which the only really unpleasant feature is its price.

F. PYGOTT.

PNEUMOCONIOSIS ABSTRACTS

Pneumoconiosis Abstracts. Volume II. Reprinted from the *Bulletin of Hygiene* for the years 1939 to 1950 inclusive, by permission of the Honorary Managing Committee of the Bureau of Hygiene and Tropical Diseases. Foreword by Charles Wilcocks. (Pp. 518. 80s.) London: Sir Isaac Pitman and Sons, Ltd. 1954.

This book is the second of two volumes in which are collected all the abstracts relating to pneumoconiosis which were published in the *Bulletin of Hygiene* from 1926 to the end of 1950. The first volume was reviewed in the *Journal* of January 2 of last year (p. 30). The second volume is arranged similarly to the first and maintains the same high standard of editing and indexing. The two volumes will be of very great value. It is to be hoped that they may be followed by further similar volumes every five years or so; the series so constituted would become an indispensable standby for all who are interested in industrial pulmonary disease.

J. G. SCADDING.

BRITISH MEDICAL JOURNAL

LONDON

SATURDAY JANUARY 15 1955.

FAMILY CENSUS

The science of demography, the study of human populations by statistical methods, makes much use of facts about mortality and fertility, two subjects of interest to medical men. As used by demographers the word "fertility" means not the ability to have children ("fecundity") but the actual occurrence of births; and, since the concern is primarily with the influence of fertility upon population, often only live births are considered. Much detailed information about the trend and pattern of fertility in Great Britain has just been published in the form of a report[1] on the Family Census of 1946, constituting the sixth and final volume of the papers of the Royal Commission on Population, which was appointed in 1944 and reported in 1949.[2]

During the nineteenth century mortality statistics aroused much interest. But fertility statistics were largely neglected until 1911, when a fertility census was undertaken as part of the general census[3]—pioneer work which threw much light on trends of fertility during the latter half of the previous century. This rather dated information, supported only by the very limited new official registration data that were becoming available as a result of the Population (Statistics) Act of 1938 and published annually in the Registrar-General's fertility tables, was insufficient for the Royal Commission, which on the recommendation of its Statistics Committee therefore undertook an *ad hoc* sample inquiry into the fertility of British women: the Commission published some of the preliminary results in one of its earlier papers.[4]

The Family Census was undertaken during January and February, 1946. A random 10% sample was selected, from food office and national registration records, of women who were or had been married, and they were sent a questionary about date of first marriage, the number and date of birth of their liveborn children, and occupation of husband. Of the million or so women asked to supply such information some 87% responded, a remarkably successful achievement in a voluntary inquiry of this kind. No serious bias was found as a result of the sampling or the failure of 13% of women to co-operate, and it was considered that the resulting data could be safely used for the study of fertility movements and patterns in Great Britain. The two-part report just published consists of some 300 pages of commentary and about 800 tables, preceded by an admirably succinct and informative summary chapter presenting the main findings. The picture that emerges now provides a national pattern with which can be compared the results of such local studies as that in Luton in 1945.[5]

From an analysis of the experience of women with completed families, comprising, more or less, women married twenty years or more before the Family Census, the outstanding and not unexpected picture that emerged was one of diminishing family size. The average completed family of a woman married in 1870–9 was 5.8 children; and, of a woman married in 1925, 2.2 children. Of marriages in 1870–9, 8% were childless, at all events as regards liveborn children, a proportion which became double for 1925 marriages. Completed families of five or more children formed 60% of the total from 1870–9 marriages but only 11% from marriages in 1925, of which half of the families so far produced consisted only of one or two children. One of the factors that much influences fertility is age at marriage: a woman marrying for the first time at the age of 40 has little time left to produce a large family. This effect of age has remained fairly stable up to the time of the Family Census, though with some lessening in relative age differences among more recent marriages compared with earlier ones. Continuously there has been a low level of childlessness among women marrying under the age of 20, for the reason that many of them are already pregnant when they marry. Other factors that influence fertility are occupation and social status, something that was known to demographers as long ago as the seventeenth century,[6] and in the analysis of the results of the Family Census nine "social status" categories have been based on husband's occupation. Relatively, the differences in family size between the various categories have remained little changed between marriages at the very

[1] Glass, D. V., and Grebenik, E., *The Trend and Pattern of Fertility in Great Britain*. A Report on the Family Census of 1946. Papers of the Royal Commission on Population, Vol. VI, Part I Report, Part II Tables. 1954. H.M.S.O. 70s.

[2] Royal Commission on Population. 1949. Report. H.M.S.O.

[3] *Census of England and Wales, 1911*. Vol. XIII, Fertility of Marriage. Part I (1917). Part II (1923). H.M.S.O.

[4] Glass, D., and Grebenik, E., *The Family Census: a Preliminary Report*. Vol. II, Reports and Selected Papers of the Statistics Committee of the Royal Commission on Population. 1950. H.M.S.O.

[5] Titmuss, R. M., and Grundy, F., *Lancet*, 1946, **2**, 687.

[6] Kuczynski, R. R., *Ann. Eugen. (Camb.)*, 1934–5, **6**, 139.

[7] Stevenson, T. H. C., *J. Roy. stat. Soc.*, 1920, **83**, 401.

beginning of this century and in 1925, fertility being highest amongst labourers, agricultural workers, and manual wage earners, intermediate for farmers and farm managers, and low for professional, salaried, and other non-manual workers. The general situation remains similar to that described by Stevenson[7] from his examination of the results of the 1911 Fertility Census. Differences in the age at marriage between different occupational groups do not account for the different levels of fertility. For example, farmers' wives marry later than the wives of other non-manual workers (with which farmers are grouped), yet have considerably larger families. If people in different occupations all married at the same average age, they would still not have the same average size of family.

The request for information about the dates of birth of children, omitted in 1911 but introduced in 1946, gave results which allowed the study of family trends and patterns to be brought up to date, freed the authors from being confined only to the study of completed families, and even permitted them to make some tentative forecasts for the future. In addition it has provided some information about spacing of births. The decline in family size has been characterized more by compression of the span of years during which children of a marriage have been born than by more widespread spacing; that is to say, women complete their families earlier in their marriage than they did formerly. The interval between marriage and first live birth is closely related to the ultimate size of the family. For marriages in 1920–4 this interval was 27 months for families totalling only the one child, and 13 months for families ultimately totalling four liveborn children. The decline in childbearing has been greatest at the later stages of married life (within the childbearing ages), and this decline in fertility with increasing length of married life is especially marked among women of the non-manual occupational groups. In considering the future trend of family size, the authors point out that examination of the data suggests that family limitation is now more widespread in Britain than had been previously estimated, and that further reductions in family size are unlikely to occur simply through the extension of family planning; nor will possible improvements in contraceptive techniques be likely to have much effect.

Analysis of the results of this Family Census suggests that a new stability in family size has been established in recent years, but accompanied throughout the community by the spread of a small family pattern. There is nothing to suggest a change from this pattern in the near future.

RUGBY FOOTBALL INJURIES

In a notable review of 590 cases of injuries sustained by Rugby football players, Mr. T. C. J. O'Connell,[1] of St. Vincent's Hospital, Dublin, analyses various types of injury observed by himself and his colleagues during twenty years of close association with the game in Ireland. Among these injuries were 129 to the head, 110 to the shoulder, 77 to the remainder of the upper limb, 75 to the knee (ligaments and cartilages), 42 to the ankle (ligaments), and 35 to the spine and pelvis. In addition, there were 53 fractures of the lower limb. He records also four fatalities—three from fracture dislocation of cervical vertebrae (through charging into or collapse of the scrum) and one from an undiagnosed rupture of the spleen.

In the last thirty years the popularity of Rugby football has led to the widespread growth of clubs whose members come from more varying walks of life than heretofore. Those who now play on Saturday afternoons, instead of being drawn mainly from public school, Services, and university circles, as was the case in the early part of the century, now include artisans, students, young businessmen, manual workers, and members of professions; and to all of them the economic aspect of injuries is one of great importance. Employers nowadays are often less inclined to take a lenient view of absences due to injuries sustained while playing games, and most Rugby players would welcome any action that can be taken to prevent or mitigate severe injuries, relatively infrequent though they may be.

Risks arising from faulty equipment, such as buckles on clothing, bad boots, poor studs, and insufficient protection for shoulders and shins could be easily eliminated. Flexible, snugly fitting boots with toe-caps that are not too heavily reinforced will do much to prevent awkward ankle injuries, for they can then be laced up quite firmly, while detachable studs of rubber or aluminium, that can be varied for dry and wet weather, are much less dangerous to other players than the leather ones that are apt to become conical in wear and sometimes develop protruding nails. Footwork in Rugby is done mainly by means of the arch and instep, so reinforced toes and steel-plated soles, so beloved by bootmakers, are more of a hindrance than a help.

Protective clothing such as is worn by American footballers hardly seems justified for our game, but O'Connell advocates shoulder protection for forwards, either by reinforcement of the acromio-

[1] *J. Irish med. Ass.*, 1954, **34**, 20.

clavicular area of the jersey (by extra layers of material such as quilting) or by providing pockets into which thin sponge-rubber pads can be slipped to cover the same area. This undoubtedly does ease the friction in the scrummage and might also help to diminish the frequency with which outsides sustain a fractured clavicle or acromio-clavicular strain from falling on the point of the shoulder. A "sweat band" made of broad elastic worn around the forehead and over the ears will protect the ears of forwards, who periodically suffer from haematoma or rupture of the ear cartilage. This is infinitely preferable to the cumbersome, old-fashioned scrum-cap, which often blocks the meatus with its flaps and causes discomfort to the cheeks and chin with its tapes. Shin guards should not be considered as "cissy," and are almost essential for front-row forwards; but they must be light and not made from material which becomes sodden and heavy in wet weather: felt is preferable to leather and sponge rubber better than either, especially if cut to shape and attached by elastic loops above the calf and beneath the instep. Well-fitting clothing can be a protection in itself, and the player with flapping waistbands and dangling stockings is often his own worst enemy.

O'Connell rightly stresses the importance of maintaining muscle tone. "Taking up the slack" is by far the most important measure in the prevention of serious injuries, and also in the restoration of fitness after injury. The strength of joints does not depend on ligaments, but on the firm bunch of muscles above and below. Too often the injured player attempts to return to the game before fully regaining muscular tone, lays himself open to further damage, and becomes accident prone. Nor should any player take part in a game if he is feverish or has a septic infection, for serious damage can be caused thereby. The custom of going on to the field for a kick-about before the game, sometimes even before changing, was a useful insurance against injury, and it is a pity that it seems to have become unfashionable.

Many strains and muscle injuries occur in ill-trained individuals early in the game in cold weather. Few spectators who saw a recent international game played in a snow-storm at Twickenham after a six weeks' interval from play due to frost will forget the spate of cramps and muscle pulls that occurred during and after that game. It clearly showed that the only real training for Rugby football is Rugby football.

Moving from a consideration of the player to the obstructions on the field, O'Connell suggests that the lower end of the goal-posts might be padded, as is the custom on some New Zealand grounds, and that corner flags should be made of thick rubber or similar yielding material that does not splinter on impact. These are wise precautions which could easily be adopted. The Saturday afternoon player is often apt to leave treatment of minor injuries over for two or three days, thus prolonging recovery. First-aid boxes should be in every pavilion, and an "accident treatment centre" open at week-ends in the large urban centres would be of great value to players who find that an injury is more serious than they thought it was in the heat of the game. O'Connell quotes one case of fatal tetanus, and there have been others in which early treatment (or, better still, prophylactic immunization) might have saved life.

TUBERCULOUS MESENTERIC ADENITIS IN CHILDREN

The King's evil—scrofula—was a common complaint in children during the last century and the first quarter of this, but has now largely disappeared. Out-patient departments are no longer crowded with children with chronically discharging sinuses and red, boggy swellings in the neck, and operating-lists in the theatres of children's hospitals no longer consist of cases for excision or curettage of cervical glands—previously an almost regular feature. Similarly, tuberculous peritonitis, which was as common in the medical wards as scrofula in the surgical wards, is now a rarity. Improvements in hygiene and particularly in the heat treatment of milk—especially pasteurization in urban areas—have been responsible for this change.

The primary tuberculosis still to be seen in children is usually intrathoracic, although a primary abdominal focus is by no means rare, especially in rural areas, for pasteurization is not yet carried out in all of them. In such areas cases of primary abdominal infection may rank nearly as high as intrathoracic. It is not always easy to diagnose tuberculous mesenteric adenitis, as Dr. H. R. E. Wallis shows in an article at p. 128 of the *Journal* this week. He lists thirteen differential diagnoses apart from all the cases of "P.U.O." Recurring abdominal pain is the predominant symptom; it may be colicky or aching in character—more commonly it is colicky—and the bouts may be accompanied by fever. Although the prognosis in Wallis's series was generally good, nevertheless fatal tuberculous meningitis can follow a primary abdominal focus just as readily as it can a primary intrathoracic focus, and the ingestion of raw milk—even in small quantities—by

infants and young children is to be condemned as a means of immunization against tuberculosis. The use of an attenuated organism such as B.C.G. is a more rational approach. Wallis rightly points out that calcification in the abdominal glands, while evidence of a tuberculous infection, is not necessarily evidence of complete healing; but, although he says that isoniazid, for example, is not necessary in treatment, it is always possible that it may become necessary. Tuberculous mesenteric adenitis is usually benign, and all will agree, therefore, that the routine giving of tuberculostatic drugs is both unnecessary and unwise. In view of the difficulty sometimes encountered in making a diagnosis the family doctor may well wonder whether he should have the abdomen *x*-rayed. This would entail considerable time and expense, and a simple tuberculin test is the real prerequisite to the diagnosis. If this is negative, no tuberculous calcification in the mesenteric glands will be found. Only those children reacting positively will need to have an *x*-ray examination. It would be interesting to know the findings of Russian paediatricians on the symptomatology of intra-abdominal calcification, for all infants in the U.S.S.R. are given B.C.G. orally at intervals, and there must be many thousands of children who now have calcified mesenteric glands.

Whether the pain is caused by pressure or by the drag of the calcified glands on the mesentery is not clear. Certainly such glands are found by chance in many children being *x*-rayed for some other condition—an intravenous pyelogram, for example—in whom there have been no abdominal symptoms at all. Clearly not all cases with these symptoms and calcified glands are necessarily suffering from active tuberculous adenitis. The other symptoms described in this condition—for example, vomiting, sweating, lassitude, and loss of weight—are likely to be connected with some activity of the tuberculous process, and it is in children with such symptoms who also have fever and a raised sedimentation rate that the use of isoniazid may have to be considered. The association of pain and vomiting with slight fever must often raise the question of appendicitis. In any doubtful case laparotomy should always be undertaken. A radiograph of the abdomen showing calcification is no guarantee that acute appendicitis is not present, and it would be most unwise to wait for 48 hours to see the result of a tuberculin test. Of the physical signs of tuberculous mesenteric adenitis, local tenderness and palpable masses are the most frequent, but both are more commonly due to constipation than to tuberculosis; radiographs must therefore be taken and calcification confirmed before the diagnosis can be accepted with certainty. If the diagnosis is still seriously entertained in the absence of any visible calcification, a negative tuberculin test will exclude the condition.

STERILIZATION METHODS

The Report of the Central Pathology Committee of the Ministry of Health on the Sterilization of Hospital Equipment, issued to hospital authorities on December 31 last, contains directions in the light of which hospitals are invited to review their present practice, and it will serve a useful purpose. It deals chiefly with surgical equipment; "bowls, baths, bedpans and urinals, crockery and cutlery are excluded since they usually come under the direct supervision of the ward sister." Discussing autoclaving, the authors lay proper emphasis on the necessity for loose packing of fabrics, and assume that the autoclave is of a type from which only two-thirds of the air can be exhausted; they therefore recommend a double evacuation. Autoclaves now exist from which air is completely expelled by downward displacement, and some mention of the advantages of this type might have been made. For the disinfection of bedding the Report suggests that a pressure of only 5 lb. per square in. (0.35 kg. per square cm.) of steam should be used, giving after a preliminary 20 in. (50 cm.) vacuum a temperature of 100° C. This is a reasonable compromise to minimize shrinkage of blankets and other damage. The Report does not discuss the circumstances calling for this treatment, and as much damage could perhaps be prevented by stopping unnecessary disinfection as by modifying the method. It is clearly necessary for the bedding of a septic or infectious case, but in many hospitals disinfection is practised after death from any cause and in all cases of cancer, a proceeding based rather on sentiment than on any scientific reasoning. The Report gives a full account of methods for the care and sterilization of syringes and needles: autoclaving and a dry oven at 160° C. are given as alternative methods, without the expression of a preference for either. It mentions that the performance of any dry oven must be checked, but not that some types may have very wide variations in temperature between one part and another. The recent experiments of E. M. Darmady and Barrington Brock,[1] made by inserting thermocouples at multiple points in ovens of different types and thus obtaining a continuous record of temperature rise, seem to show that gas-heated

[1] *J. clin. Path.*, 1954, 7, 290.
[2] *The Aseptic Treatment of Wounds*. New York. 1948.
[3] *Z. Hyg. InfektKr.*, 1954, 140, 144.

ovens are most unsatisfactory, and that even those electrically heated perform consistently only when fitted with a fan to circulate the contained air. These authors also recommend loading the oven while it is hot, whereas the Report states that it should be cold.

Two of the articles in commonest use in surgery seem to occasion the greatest difficulty in sterilization. Methods for sharp instruments are the most diverse, mainly because heat in various forms is reputed to blunt them. That advocated here is boiling in 2% sodium carbonate. The procedure advocated for rubber gloves, the other troublesome article, at least in British surgical practice, is open to criticism. The report recommends that after cleaning they should first be boiled, and then, because higher temperatures spoil them, autoclaved at a pressure of only 5 lb. per square in. (0.35 kg. per square cm.). It then admits that "such treatment by itself does not ensure complete sterility so that gloves which may have become heavily contaminated with sporing bacteria, e.g., in a case of gas gangrene, should be destroyed." It seems in the first place a pity that the hoary old operating-theatre myth about the special infectivity of gas gangrene should thus be officially perpetuated. *Cl. welchii*, the principal cause of gas gangrene, is a normal inhabitant of the human lower bowel, and the precautions called for when it happens to produce infection are equally necessary after any operation on the colon, rectum, or anus. The instructions given for sterilization conflict at every point with those of C. W. Walter,[2] whose monumental work on surgical asepsis is the most complete of its kind and reflects the best American practice. He states categorically that gloves should not be boiled, because they imbibe water and thus lose tensile strength. He also states that "gloves withstand sterilization by saturated steam but deteriorate rapidly in mixtures of air and steam." In other words, what matters is not absolute temperature but the admixture with steam of hot air (presumably the damage is an oxidation effect). In an autoclave giving an atmosphere of pure steam gloves can be sterilized at 15 lb. per square in. (1 kg. per square cm.) at 121° C. It is sometimes suggested that this should be maintained for only 15 minutes, but at the Peter Bent Brigham Hospital they maintain it for 30 minutes, as in autoclaving other materials, simply for the sake of uniformity, and have no complaints about the effect on the quality of the rubber. It may be concluded from the experiments of B. Schmidt and E. Möller,[3] who compared the effects of 120° C. for 30 minutes and 134° C. for 5 minutes on the strength and elasticity of rubber gloves —slightly to the advantage of the former—that sterilization at full pressure is also the usual practice in Germany. Surely the truth in this very important matter should be finally determined, and British surgical practice brought into line with it if the facts demand a change. That gloves, of all things used in an operation, should be of doubtful sterility is intolerable. If it is a fact that hot air and not steam is what damages gloves—and anyone doubting this can test the statement by experiment—then all that is needed is an autoclave giving an atmosphere of pure steam and its use as for sterilizing any other materials.

PAPILLOMATOSIS OF THE BLADDER

The treatment of diffuse villous papillomatosis of the bladder is peculiarly difficult, since despite the simple nature of the lesions they are often present in such numbers that control by cysto-diathermy or endoscopic resection is impracticable. Moreover, a proportion of tumours appear eventually to undergo malignant changes, thus adding to the hazards of incomplete destruction by such means. Alternatively, extirpation by total cystectomy may seem unnecessarily radical in early cases, while radiotherapy from a remote source carries the disadvantage of exposing the surrounding tissues to an excessive dose of irradiation. During the last few years efforts have been made to overcome this last difficulty by devising methods of intracavitary irradiation, whereby the tumours may be treated more selectively. The use of radioactive solutions (instilled into a rubber balloon within the bladder) has allowed a diffuse irradiation of the mucosa with limited deeper penetration depending on the quality of the isotope and on the screening effect of the containing sheath. In practice, however, technical difficulties have greatly narrowed the margin of safety between securing adequate destruction of the tumour and avoiding subsequent radionecrosis of the bladder wall. On the one hand the rubber sheath has discriminated unfavourably in reducing the surface dose (while permitting the passage of more penetrating rays), and on the other hand the tumour has been pressed against the bladder wall, thus permitting only one surface to be fully irradiated.

Elsewhere in this issue Dr. Frank Ellis and Mr. R. Oliver describe a modification of radiotherapy which gives promise of proving both safe and effective in the treatment of superficial papillomatosis. The essential difference in their technique lies in the direct instillation of a radioactive solution into the bladder, thus allowing the papillomata to float out and become exposed to irradiation from all sides. At the same time the screening effect of the catheter bag is eliminated and the overall dosage can thus be reduced to avoid an excessive dose in depth. Preliminary work has indicated that, with certain precautions, a standard preparation of radioactive colloidal gold is suitable for this purpose, and may be retained within the bladder for the required time without ill effect and can be subsequently evacuated by irrigation. Using this method, the authors observed the disappearance of multiple villous tumours, and they

describe the reduction in size of neoplasms less simple in appearance, thus making easier their eradication by other means. It must be emphasized, however, that, *a priori*, the technique is unsuitable for infiltrating growths, since effective dosage would necessarily carry the risk of damage to the normal bladder wall. Experience with previous methods has shown that late necrosis and contracture may occur up to several years after treatment, and the utmost caution is therefore required in limiting the dose of irradiation lethal to the tumour to a depth of penetration scarcely exceeding the radius of a simple papillary frond. Allowance has thus to be made for the dilution of the isotope solution by urinary secretion during its retention in the bladder, and for the ability of the patient to refrain from micturition during the prescribed period. This and other matters relating to the control of radioactive materials make it essential that for the time being further trials of this method of treatment should be conducted only under carefully supervised conditions.

EYES AND APPETITE

The use of dyes in food manufacture has become so extensive that the Food Standards Committee of the Ministry of Food has recently issued a report[1] by a subcommittee on the possible hazards arising from such practices. The report, which was briefly summarized in last week's *Journal*, provides such an astonishing record of the use of colours in food that it is perhaps reasonable to wonder whether the research resources of the food manufacturing industry are being properly used. If increased reliance is being placed on colour in order to sell food, it suggests that inadequate attention is being paid to correcting processes of manufacture so that natural colour and flavour are retained to the maximum. Doubtless there are difficulties, especially if costs are to be kept low; nevertheless there would have been much support for the subcommittee if it had taken a stronger line against this ever-growing use of artificial colours in food. The manufacturers appear to have made a plea for the retention of all the colours hitherto put to use in this country and wished to include all those permitted in other countries. In this country at present there is a short list of forbidden colours, while any others may be used. The report rightly recommends that in the future there shall be a permitted list, but when the subcommittee tried to compose such a list it had many difficulties to contend with: there are 82 different colours named on 22 permitted lists of those countries that have such lists, yet only one dye is common to them all.

Largely avoiding the technological issues and subtler matters of good taste in food manufacture, the subcommittee concentrated its attention on the possible toxic hazard from consuming these dyes. Many of the colours used have never been tested for toxicity: none has any marked acute toxic effects, and all are present in very small quantities in our diet. This raises the vexed question of the possible possession of chronic toxic properties by these colours. Naturally the subcommittee paid most attention to the possibility of the dyes having carcinogenic properties. Some have already been incriminated as carcinogens for experimental animals: others are closely related to carcinogenic compounds either chemically or by derivation from them. Probably one shadow hanging over the inquiry is the known property of β-naphthylamine to produce bladder cancer in man. Little, however, is known about the doses needed to do this, and it is impossible to say whether a lifelong consumer of coloured foods will ever ingest a quantity of dye comparable to the amount needed to cause cancer in a worker in a dye factory where β-naphthylamine used to be handled. Ideally every dye on the permitted list should be tested in such a way as to exclude the fact that it is a carcinogen for a few laboratory animal species, but even so such screening tests might well have allowed β-naphthylamine itself to pass as harmless. Other tests for chronic toxicity are of doubtful value, and it seems questionable whether a battery of tests such as those outlined by Professor A. C. Frazer would be a practical proposition for 40-odd dyestuffs. Simple excretion tests if done on animals and perhaps on man might reveal a few dyes that the body excreted unchanged. Another important point made by the subcommittee is that these dyes are rarely manufactured specially for use in food, so that while shade may be crucial chemical purity is not so essential. It should surely be made compulsory that all dyes used in food should meet fairly rigid standards of chemical purity. This in turn might help to curtail the list, because some dyes would be more readily purified than others. The food manufacturers have successfully overcome the handicap of the withdrawal of many preservatives, and they should be discouraged from placing increasing reliance on artificial colours in order to make their products attractive. One of the great objections to mass-produced food is that it loses its natural flavour: artificial colouring, even if harmless, is poor compensation for loss of quality.

[1] Food Standards Committee Report on Colouring Matters: Recommendations Relating to the Use of Colouring Matters in Food, 1954. H.M.S.O., London. Price 1s. net.

EDINBURGH MEDICAL JOURNAL

The December number of this memorial to Scottish medicine has reached us with the sad news that it is the last to appear. Rising costs of production, a sluggish circulation, and diminished revenue have combined to kill a periodical whose continuous appearance since 1805 (as the *Edinburgh Medical and Surgical Journal* until 1855) has been a steady source of entertainment and instruction to British readers, and in particular to Edinburgh graduates. Since 1908 the *Edinburgh Medical Journal* has been the property of a limited company of doctors, and its reserve funds have now all been mopped up by the cumulative losses of the last few years. This notable casualty in medical periodicals is but an example of the severe financial strains to which periodical publishing is now subject. It is indeed distressing to have to record the disappearance of a journal which traces its origins directly back to *Medical Essays and Observations* (1733–44), the fourth oldest medical periodical in the United Kingdom.

EMERGENCIES IN GENERAL PRACTICE

SHOCK*

BY

Sir HENEAGE OGILVIE, K.B.E., M.D., M.Ch., F.R.C.S.

Consultant Surgeon, Guy's Hospital

The study of shock has for many years attracted the ablest investigators in Britain and America. Men like Aub, Blalock, Bywaters, Grant, Green, Gregerson, Haist, Moon, Phemister, and Wilson (the order is alphabetical rather than chronological) have paid particular attention to this problem, and by their research work in the laboratory and their clinical observations at the bedside they have added greatly to our knowledge of the reactions of the animal and human body to various forms of injury.

The treatment of shock is essentially a practical problem. We must study the research work that has been done in the laboratory, and if it has provided an answer we must apply the lesson it brings to our clinical tasks. Very often, however, the answer is "So what?" and it is extremely important that we should leave philosophic doubt behind when we come to the side of the pale listless man who has just been rushed in by the ambulance. It is right, therefore, that from time to time a clinical speaker should try before a clinical audience to bring this important subject from the laboratory to the bedside, to turn aside from a consideration of what shock might be and consider what shock is as we see it, what steps we can take to prevent it, and what we can do to save the shocked patient.

What is Shock?

We are often criticized by our scientific friends for using the word "shock" without explaining exactly what we mean by it. The word "shock" has a very definite meaning to me, and to most surgeons. To me it means a state of collapse following injury, and I shall go on calling it shock till I find I am wrong. The definitions of the experts are no more helpful than this simple statement. Blalock defines shock as "peripheral circulatory failure." Why peripheral? Why failure? In the type of shock most commonly encountered in clinical practice, that due to haemorrhage or trauma, nothing has failed. The central pump and the peripheral mechanism are working with supreme efficiency. The motor is spluttering only because the tank is running dry. Moon defines shock as "a circulatory deficiency characterized by decreased blood volume, decreased cardiac output, and increased concentration of the blood." This may be the shock of the laboratory mouse. It is not the shock of the wounded soldier; unless he is burned or crushed his blood concentration is normal or below that figure, and it falls in subsequent days. These definitions, in attempting to give an exact meaning to a comprehensive and general term, force upon it a significance foreign to its accustomed clinical use. This is hardly surprising, since many of the experiments whereby shock is produced in the laboratory bear no relation to the manner of its causation in surgical practice.

I will return to my first definition of shock and expand it slightly. "Shock is a state of collapse following injury, characterized by a depression of the circulation." All we know when we are called to the patient's side is that he has been injured, that he is collapsed, and that he lies apathetic with an ashen grey face and cold clammy hands. The diagnosis is a clinical one, and, having made it, we must set ourselves urgently to seek the cause and decide the treatment.

Mechanism of Shock

The circulation of the blood depends on three things: on the action and force of the heart beat, on the volume and viscosity of the blood, and on the peripheral resistance of the arterioles. Interference with one, two, or all of them may be found in the condition of acute circulatory depression known as shock. Heart failure may resemble shock. Many factors associated with injury, particularly with battle injury—peritonitis, blast damage to the lungs, fat embolism, acute anaerobic infection, absorption of toxins from damaged muscle—may complicate and be partly responsible for the clinical state of shock. But to label them as "shock" is to make the term completely meaningless.

Traumatic shock is, in the overwhelming majority of cases, the result of a diminution of the effective circulating volume of the blood, and the word "shock" should be used for this condition alone. The other shock-like states should be called pseudo-shock. The later changes caused in the circulatory mechanism by anoxaemia, infection, or tissue toxins of various sorts should be referred to as epiphenomena or sequelae of shock, but not as shock.

In shock the diminution of volume may be due to actual loss, or to a sudden increase in the capacity of the vascular bed, the volume being unchanged or diminished to an extent that would not in itself cause shock. In wound shock the loss is one of blood, either from the wound or into damaged tissues. In the shock which follows crush lacerations or severe surgical operations the loss is of blood and plasma. In shock from burns the loss is of plasma only, from the burned surface and into the tissues underlying it. In the vasovagal syndrome, known also as primary or nervous shock, a state which may be found alone or preceding or accompanying true oligaemic shock, the circulating volume is inadequate to the vascular bed, whose capacity is increased by widespread dilatation.

Primary and Secondary Shock

Phemister has observed that "primary and secondary shock should be recognized on the basis of difference in aetiology rather than difference in time of occurrence." Primary, or nervous, shock is a condition of circulatory disturbance associated with low blood pressure due to dilatation of the peripheral arterioles, and a slow pulse due to stimulation of the vagi. It is a cardiovascular upset of reflex origin, the result of painful stimuli or of emotional disturbance, very often a combination of the two. A painful injury is more likely to cause it than a large one, and an apprehensive individual is more likely to suffer from it than a phlegmatic one. The main features distinguishing primary from secondary shock, apart from the nature of the causative injury, are that the patient does not look ill, that his skin is warm, that he is torpid or unconscious rather than apathetic, and that his pulse is slow.

Primary shock is essentially a transient phenomenon that responds to rest, relief of pain, warmth, hot drinks, and removal from distressing surroundings, and a good response to these simple measures may be the surest method of distinguishing primary from secondary shock. It is, however, less important to recognize those who respond well than it is

* Based on a contribution to a symposium at Bristol University on "Medical Aspects of Atomic War" (see *Journal*, November 27, 1954, p. 1283).

to watch anxiously for those who do not or who relapse after temporary improvement, for they are suffering from secondary shock and need immediate and active treatment. If there is any doubt, needless transfusion of a patient in primary shock is a harmless mistake compared with delay in starting the transfusion of one suffering from secondary shock.

Secondary shock must be assumed where there has been much blood loss or tissue damage. Some estimate of the loss can often be made from the history given by the patient or his friends, or from observing the amount of blood on the clothing or the stretcher. But fluid may be lost into the tissues without external loss, a mechanism repeatedly stressed by Blalock. A man can bleed to death into the thigh muscles round a fractured femur without any free haemorrhage occurring. Grant, in his observations on wound shock in the Italian campaign published in 1951 in the Medical Research Council Special Report Series, No. 277, has pointed out that the amount of blood and plasma lost into the damaged tissues in extensive muscle injuries is far greater than had been previously realized, and that the loss continues and is responsible for a relapse into clinical shock after resuscitation. The view that shock leads to endothelial damage, with loss of fluid into tissue spaces throughout the body and concentration of corpuscles in the peripheral capillaries, is no longer held.

Assessment of the Shocked Patient

A man suffering from shock looks ill. His attitude is apathetic, but he is mentally alert and answers questions readily. His skin is cold, moist, and pale, with a greyish colour, particularly about the ears and lips. His hands and feet are icy cold. His eyes, with pupils dilated, appear abnormally bright. His respirations are little altered. The pulse is rapid and of low tension. He passes little urine, and is prone to vomit any fluids given by mouth. Air-hunger and spontaneous vomiting are indications of severe shock.

An index to the presence and degree of shock, but not an entirely reliable one, is the blood pressure. While the fall in systolic pressure is usually commensurate with the loss of blood volume and the degree of shock, there are surprising exceptions. Some men show a low blood pressure rising subsequently, some show periodic rises and falls, and some maintain a high pressure till just before the end. A low pulse pressure is often of more significance than a low systolic pressure.

The whole clinical picture of shock can usually be accounted for by the loss of circulating fluid alone. The degree of shock is roughly proportional to the loss of fluid : a loss of 2 pints (1 litre) leads to moderate shock, one of 3 pints (1.5 litres) to severe shock, one of 4 pints (2 litres) (roughly 40% of the blood volume) to profound shock. A known loss of 4 pints (2 litres), even though the patient may, by supremely efficient compensation, be able temporarily to keep his blood pressure up, will eventually lead to profound shock, and, conversely, profound shock means that at least 4 pints (2 litres) have been lost and must be replaced.

Restoration of the Circulation

The treatment of oligaemic shock is the restoration of the circulating volume to its former level. If possible, the volume should be restored qualitatively as well as quantitatively—that is, lost blood should be replaced with blood, and plasma with plasma—but the immediate need is for volume, and the fluid must usually be introduced directly into the circulation. Water by mouth or by rectum or crystalloid fluids intravenously are of little value when the circulatory loss has been large enough to give rise to clinically recognizable shock ; under such conditions water is poorly absorbed in the alimentary canal and poorly retained in the circulatory system.

The restoration of volume should be early and rapid. While a patient is in a state of shock, all his tissues are poorly supplied with oxygen ; organs such as the kidneys and liver are by-passed to conserve blood for the heart and brain and may suffer permanent damage, and bacteria in his wounds, particularly the anaerobes, are given a chance to establish themselves. When a total of 4 pints (2 litres) or more is needed, the first two should be run in rapidly, using pressure to assist gravity, and full restoration in four hours should be aimed at.

The choice between blood and plasma depends to some extent on the availability of the two. Plasma can always be obtained, blood only when donors have been prepared, and blood in quantity only when arrangements have been made to supply it. Plasma is free from the dangers of reaction due to incompatibility, infection, or mechanical destruction of the red cells which are present with blood, but may transmit the virus of hepatitis. It is better than blood for the shock of burns, indeed for all shock characterized by haemoconcentration. In haemorrhage it is as good as blood for restoring volume, and not greatly inferior in therapeutic results when the blood loss has been moderate. It flows more easily, so that even in transfusion for severe haemorrhage it has been advised that plasma should be used for the first 2 pints (1 litre), which are given rapidly. Blood should be used to replace a haemorrhage of more than 2 pints (1 litre), and when the haemorrhage is not merely severe but is expected to continue during resuscitation or operation, blood alone should be used. Plasma cannot bring a man who has lost more than 2 pints (1 litre) of blood into a state fit to withstand a severe operation, or enable him to overcome infection or to repulse anaerobes.

"Plasma-savers" are solutions containing large molecules —of gum acacia, a polyvinyl compound, or a polysaccharide —that remain in the circulation and can replace in volume and viscosity an equal amount of blood. What is their place in the treatment of shock ? The answer is in the seventh chapter of St. Matthew's Gospel : "What man is there of you, whom if his son ask bread, will he give him a stone ?" The plasma-savers provide volume and viscosity and can restore the blood pressure, but they do not carry oxygen, and they do not provide energy or any substance used by the body. On the other hand, they tend to clump the red cells, thus interfering with grouping, and they are finally fixed by the reticulo-endothelial system. By restoring the blood pressure before the cause of hypotension has been arrested, they may restart a haemorrhage that has stopped and wash out the life fluid with a fake substitute.

There is one legitimate place for the plasma-savers : to keep a patient alive in a desperate emergency till blood or plasma can be obtained. If a man has lost 5 pints (2.8 litres) of blood rapidly, or if his systolic pressure has dropped to 50 mm., his central nervous system and his kidneys will suffer irreparable damage and his acid-base equilibrium will be upset beyond recovery unless the pressure can be raised within half an hour. Plasma-savers must be given till blood arrives, for desperate situations demand desperate remedies.

I hold that every surgeon who is called upon to treat acute injuries in healthy men should act upon the belief that no haemorrhage need be fatal if it can be stopped and the lost blood can be replaced early enough and fast enough, and no shock need become irreversible if it can be reversed in time and with sufficient energy. Shock becomes irreversible chiefly because prolonged anoxia has been allowed to wreck the machinery of recovery. Many more lives are lost by tardy, hesitant, or inadequate transfusion than by excessive transfusion or transfusion for the wrong indications.

Ancillary Measures

I must touch briefly on some of the other measures used in the treatment of shock. Warmth may be beneficial in primary shock, but in secondary shock it is harmful. Experimentally shocked animals are more likely to die in a warm room than in a cold one. The cold skin of shock is an index of a peripheral vasoconstriction the purpose of which is to reduce the volume of the vascular bed and to maintain

the arterial pressure, and a drop in body temperature is beneficial in reducing the general metabolism to a level more adapted to the reduced oxygen-carrying capacity of the blood. The "shock-cradle" can be a shock producer. Patients expend their ebbing strength in trying to throw it off, and in this demonstrate that the physiological call of instinct is wiser than the teaching of the textbooks.

Morphine must be used with great caution. No more than ¼ gr. (16 mg.) should be given at a time, and it should be given into a vein, since in a state of shock it is absorbed slowly from the subcutaneous tissues. A second and larger subcutaneous dose is apt to be given if the first fails, and when later the circulation is restored the accumulated amount is absorbed and may produce a profound stupor.

The use of pressor drugs, including the adrenal preparations, is unwise. They may do good in primary shock accompanied by vasodilatation, but here they are unnecessary. In oligaemic shock, which is associated with vasoconstriction, the real need is for an increased supply of blood and oxygen to the tissues rather than for a raised systolic pressure, and further vasoconstriction may therefore do more harm than good.

When Normal Services Fail

The treatment I have discussed demands, not necessarily hospital conditions, but at any rate facilities for careful examination and constant supervision, the provision of shelter and bed-clothing, and a supply of the necessary fluids, drugs, and apparatus.

Should a casualty be moved to hospital before shock has been combated? A man in profound shock can easily be killed by a rough journey, particularly if his fractures are not adequately splinted. But part of the shock seen immediately after an accident is nervous in origin, and the patient will recover considerably after a short period of rest during which he is kept warm, reassured, and given fluids. The apparatus for intravenous fluid replacement is seldom available at the scene of an accident, but it may arrive with the ambulance. Should blood or dextran be given before the casualty is loaded for the journey? The answer depends on the state of the patient, the nature of the injury, and the length and quality of the coming journey. When in doubt it is better not to transfuse, for transfusion without control of the blood loss is apt to increase that loss, particularly if it raises the blood pressure above shock level during a bumpy trip. However, if the bleeding can be controlled by ligature or tourniquet, it may be wise to start transfusion before the man is put into the ambulance, and to send him off, with the transfusion running, as soon as a palpable pulse has returned.

What should be done in a major disaster when normal services are absent, inadequate, or disrupted? Three things that can be given to all are reassurance, warmth, and fluids. Reassurance alone will restore most cases of primary shock and benefit all. No one can dispense it better than the doctor, who by his quiet confident actions can do most to assure the victims that the crisis is over and the situation is in hand. Warmth and fluids must be dispensed with more caution, but here, fortunately, the customer is always right. The man who feels cold needs blankets. The man who is cold and does not feel it is better left uncovered. With water, also, personal desires can usually be trusted; the man who asks for a drink can usually be given one, the man who does not want water or vomits when it is given him should be left alone or given fluids another way. Pain must be allayed if the means are available, and morphine, given intravenously, is the best analgesic in shock. The administration of blood plasma and dextran will depend on whether these fluids are available; they cannot be improvised on the spot.

We must always remember that even the most severe shock is not necessarily fatal. Men have recovered after lying out all night on an icy battlefield who might have died had they been found earlier and subjected to the additional trauma of movement. The one thing that must be remembered is that a shocked man will not stand an anaesthetic or an operation, and if the means of treating shock actively are not available he will stand a better chance if nothing is done to his injuries beyond splinting fractures, stopping haemorrhage, dressing his wounds, and keeping infection at bay by the administration of sulphonamides at regular intervals, than if he is subjected to surgical excision of wounds and mechanical cleansing of burns while still in a state of shock.

Next article on Emergencies in General Practice.—"The Differential Diagnosis of Coma," by Dr. M. J. Parsonage.

Refresher Course Books.—Copies of the first two volumes of collected articles from the Refresher Course for General Practitioners published in the *Journal* are still available at 25s. (postage 1s.) each. The first volume contains 55 articles and the second 60. Each article has been revised and brought up to date by its author.

These books may be obtained from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or through any bookseller.

BACTERIAL GENETICS

[FROM A SPECIAL CORRESPONDENT]

An informal meeting on bacterial genetics was held at the London School of Hygiene and Tropical Medicine from December 14 to 17, 1954. The intention was to provide reviews of the main topics in terms comprehensible to those not well acquainted with the subject, and for the most part the speakers succeeded reasonably well.

Experimental Production of New Strains

The first day was devoted to some of the methods by which two bacterial strains can interact to produce a new "hybrid" strain. In the pneumococcus, the influenza bacillus (*Haem. influenzae*), and the meningococcus, cells treated with deoxyribonucleic acid (D.N.A.) extracted from some other strain of the same species may acquire some heritable character from that strain. Many different traits can be transferred in this way; and it has recently been discovered that some pairs of traits are linked—that is, that absorption of a single particle of D.N.A. by a bacterium may confer on it two distinct new hereditary properties. These facts make it at least very probable that D.N.A. constitutes the genetic apparatus of the bacteria concerned, and that single macromolecules of D.N.A. contain differentiated regions regulating different bacterial characters—that is, different genes. The latest development in this field was reported from the Biophysics Research Unit at King's College, London. By chromatography on a column of histone adsorbed on kieselguhr it has been possible to divide D.N.A. from streptomycin-resistant pneumococci into a series of fractions which differ not only in their chemical composition (ratio of bases) but also in their ability to transform streptomycin-sensitive pneumococci into resistant ones. It remains to be seen whether the ability to effect different transformations will be found concentrated in a single fraction or distributed amongst different ones. In the latter case the isolation and chemical characterization of a specific gene may not be quite so remote a possibility as it has hitherto seemed.

The recently discovered phenomenon of transduction of characters from one salmonella strain to cells of another by treatment with a cell-free filtrate of a lysed culture now appears in essence similar to the D.N.A.-mediated transformations; the main difference being that in salmonella the genetic material requires a phage particle to carry it across from the lysed cells to the cells of the recipient strain. The chemical nature of this phage-transported salmonella

genetic material is unknown, but it seems likely that it also is D.N.A., present as contaminant material within the shell of the phage particle, and protected by its situation from deoxyribonuclease, which inactivates free D.N.A. but not the transducing activity of phage-lysed salmonella cultures.

Mating

Genetic recombination in *Bact. coli K12* was reviewed by Dr. W. HAYES, of the Postgraduate Medical School of London. In this organism pairs of strains can be crossed, but only if the cells of the two strains are allowed to come into direct contact. In this respect the process resembles sexuality in higher organisms, but many anomalies await explanation. In particular, most of the recombinants derive the great majority of their characters from but one of the two parent strains—that is, from the strain described as *F*—, since it lacks the "fertility factor," *F*, which must be present in at least one parent strain if a crossing is to be fertile. The *F* factor may be a phage-like particle which carries across a variable amount of bacterial genetic material from an *F*+ cell to an *F*— cell with which it has fused, or it may be an "elimination locus" on the bacterial linkage group which commonly causes loss of a segment of this group after formation of a normal zygote. Dr. J. L. JINKS, of the University of Birmingham, presented a new analysis, based on the latter hypothesis, which, he stated, provides a satisfactory explanation both for his own recombination data and for all earlier data published by others. Fuller details of this work will be awaited with interest. The nature of the *F* agent is one of the most interesting problems in bacterial genetics. One of its more surprising properties is that *F*— cells readily acquire the *F*+ character if grown in mixed culture with *F*+ cells, but that they cannot be made *F*+ by treatment with any cell-free extract of *F*+ cells. If the *F* agent is indeed a particle transmissible by infection, it seems that direct cell contact is required for infection to occur.

Bact. coli K12 continues to provide surprises for the bacterial geneticist. It has been known for some time that many, but not all, sub-lines of this strain are lysogenic for a phage called λ, and that active growth of the latent phage, and lysis of the cell, can be induced by ultra-violet irradiation. Recent work in Paris shows that, when a lysogenic strain carrying the *F* factor (or its variant form called *Hfr.*) is mixed with a non-lysogenic *F*— strain, many cells lyse and liberate phage λ, and it has been proved that this results not from infection of non-lysogenic cells by free phage but from transfer of latent phage or pro-phage into sensitive cells by cell fusion (or adhesion). In matings of this kind it seems that many or most of the pairs of mating cells, and so of the potential recombinants also, are lost through this "erotic induction" of the active growth of latent phage. In other work on K12, the inheritance of lysogenicity has been studied, using precautions to avoid induction of phage activity. The property of lysogenicity behaves as though it resided at a particular locus in the bacterial linkage group, and there now seems little reason to doubt that the genetic material of the carried phage is in fact attached to, or incorporated in, the linkage group of the host at this locus, and that the pro-phage or latent phage is indeed "a parasite at the genetic level."

From the discussion on the genetics of bacteriophage it appeared that it has been established that phage particles contain a series of mutable genes which are arranged in one or more linear linkage groups, as in higher organisms, and that after infection of a cell by more than one particle of differing genotype recombination may occur. A model based on the hypothesis that recombination results from a series of matings of pairs of particles, with mutual exchange of genes, so as to produce two recombinants per mating, accounts satisfactorily for the experimental data. But another model proposes that a single recombinant arises as a result of replication in part of one "parent" particle and in part of another, so that a pairing produces one recombinant only, not two of complementary composition, and this model also is said to be satisfactory. It seems that the bacterial cell conceals unexpectedly well the essential nature of the sexual or parasexual process in bacteriophage.

Bacterial Adaptation

One session was devoted to a discussion of bacterial adaptation. Sir CYRIL HINSHELWOOD, F.R.S., gave a brief exposition of his well-known theory which provides a satisfactory explanation for the inheritance of acquired characters in bacteria. It now appears that in this controversial field all parties are agreed that some spontaneous mutations occur, and that some adaptive changes are specifically induced by the environment. The one disagreement is on the interpretation of the experiments which purport to show that specifically induced adaptive changes are inherited in the absence of the stimulus which provoked them.

Virulence

In a session on the applications of bacterial genetics much attention was devoted to the virulence of bacterial pathogens. Dr. T. W. BURROWS, of Porton, discussed some of the characters required by an organism to make it a success as a disease-producer. One such character is the ability to grow in an environment of the chemical composition of the tissue fluids of the host, and he has shown that this character may be successfully investigated at the genetic level. In a strain of *Salmonella typhi* most nutritionally exacting mutants were of about the same mouse-virulence as the parent strain, but mutants needing to be supplied with purines to enable them to grow were almost or entirely avirulent; and it appears that this is because the peritoneal fluid of the mouse does not contain enough purines for the needs of the mutant bacterium. Administration of purines to the host enables the bacteria to multiply and kill it, and loss of the exacting character by back-mutation restores the original virulence. This constitutes a new instance of the loss (and regain) of virulence as a result of alteration of a single gene regulating a character indispensable for virulence. It is noteworthy that the first instance of bacterial hybridization—that is, the type-transformation of pneumococci discovered by Griffith in 1928—was detected by study of another such character, encapsulation. Dr. D. ROWLEY, of the Wright-Fleming Institute, presented new data on the mechanism of the differing virulence for mice of two strains of *Bact. coli* of the same serological type. His experiments indicate that the difference in virulence results from the susceptibility of one strain, and the resistance of the other, to the bactericidal action of complement and properdin, in the absence of specific antibody. The genetic basis of this difference remains to be discovered.

Dr. L. F. HEWITT described work on the conversion of non-toxigenic diphtheria strains to toxigenicity by treatment with certain phages. So far as can be judged at present, it seems that the process involved is neither genetic transfer nor the selection of spontaneous mutants, but a specific effect of lysogenization with certain phages on the metabolism of the host. This is the only known instance of such a consequence of the lysogenic state, and its mechanism is unexplained.

Population Studies

The population genetics of bacteria was briefly reviewed by Dr. P. ARMITAGE. In this field theoretical analysis has now provided adequate explanations for much that has been observed on bacterial cultures growing *in vitro*; the more difficult problems of changes in virulence of bacterial pathogens under natural conditions, and of the forces tending to maintain the constancy of bacterial characters in the wild, remain as yet little studied. Their importance for medicine is emphasized by, for instance, the increasing proportion of antibiotic-resistant strains in some bacterial species harboured by certain human populations.

In closing the meeting, Professor J. B. S. HALDANE, F.R.S., envied the microbiologists the rapidity with which they could obtain results in genetic experiments, and drew attention

to various parallel problems in the genetics of micro-organisms and of larger plants and animals. He contrasted the variety of mechanisms by which recombination of hereditary characters could occur in bacteria with the almost exclusive reliance of the metazoans on sexuality. He congratulated the microbiologists on their grasp of "classical" genetics, but regretted the absence of a control world in which the discoveries of microbial genetics would have had to be interpreted without preconceived notions; for this, he felt, might have produced useful new ideas. To the writer, however, it seems that until recent years most bacteriologists did indeed interpret their results in just such ignorance of the genetics of sexual organisms, and that the process was on the whole a very barren one.

SOCIAL PROBLEMS OF THE YOUNG DISABLED

A study of a cross-section of disabled persons aged 15–45 is the subject of a report to the Leverhulme Research Awards and the South-east Metropolitan Regional Hospital Board by Mrs. M. U. SHARP, a member of the Association of General and Family Case-workers. Thanks to the co-operation of the Kent County Council, certain voluntary societies, the National Assistance Board, and the Ministries of Pensions and of Labour, Mrs. Sharp has been able to get in touch with over 400 disabled persons in Kent, a few of them long-stay patients in hospital, but by far the greater number at home or in some institution. They were suffering from various incapacitating diseases—most of them from anterior poliomyelitis and polioencephalitis, spastic diplegia, disseminated sclerosis, and rheumatoid arthritis.

Mrs. Sharp was impressed by the need for grouping the younger patients together in small special units. Of the 354 persons in their own homes or in institutional care, about 210 were so severely handicapped as to make life a major problem for them. She found in the homes of many of these disabled persons a tendency for relatives to be too protective—an attitude responsible in some cases for preventing young people from going away for training or employment. She also makes the useful suggestion that certain gadgets which make life easier for such persons in dressing, toilet, and feeding should be supplied under the National Health Service. Such gadgets lighten the task both of the relatives and of the disabled person himself to a surprising degree, and the National Association for the Paralysed has published a useful handbook on them. But unless the patient is in a hospital which has a physical medicine department it is very difficult for him to obtain the requisite gadgets. They might well be scheduled appliances. Loneliness and idleness are the bane of the handicapped. Mrs. Sharp in her survey of the 400 persons found about 30 who needed some diversional occupation but could not make saleable products, and about 60 who could do really good handiwork but lacked a suitable market. She states that the home workers' scheme of Remploy Limited requires for home work that the disabled should work at least 30 to 35 hours a week, have two good hands and good eyes, and be prepared when trained to come off their benefits. Many people covered by her survey were incapable of sustained effort for so long, and were not prepared to risk the loss of an assured source of income.

One of several recommendations which she makes is that section 29 of the National Assistance Act, concerning welfare services for handicapped persons other than the blind and partially sighted, should be made obligatory on local authorities rather than permissive; and that welfare committees, in conjunction with county education committees, should pay special attention to the future needs of children still at school who will require institutional care, and should arrange an aftercare service for those who are considered unsuitable for either training or employment on returning to their homes.

Correspondence

Low Backache

SIR,—Dr. L. S. Calvert (*Journal*, December 18, 1954, p. 1488) makes a plea for the enlargement of departments of physical medicine to treat chronic backache. His letter suggests that orthopaedic surgeons are failing in their responsibility for dealing with backache, and that, moreover, they are tending to a dog-in-the-manger attitude. There must be many, doctors and patients alike, who share Dr. Calvert's concern, and it seems necessary that steps should be taken to attempt to teach the public "the facts about backache" so that they may know what they are entitled to expect, or not to expect, from an enlightened, humane, and sympathetic Health Service.

If the taxpayer is to foot the bill for the treatment of the backaches of his fellow citizens, he is surely justified in expecting the medical profession to be unanimous on the following three points: (1) that in the majority of cases there is a significant organic cause; (2) that the rationale of treatment is scientifically sound; and (3) that the results of treatment are worth the financial outlay, either in terms of crude economics or as a gift to human happiness. The experience of orthopaedic surgeons, with all the technique of physical medicine at their disposal, as well as many others not available to physiotherapists, suggests that these three criteria are satisfied only in a minority of cases. It is to the credit of orthopaedic surgery that it does not pamper every ache and pain in the community which the setting up of increased facilities for physical medicine undoubtedly would encourage.

The orthopaedic surgeon faces the backaching multitudes with five principal ideas in mind: (1) to make a diagnosis and, as far as possible, to exclude early and serious diseases masquerading as "low back pain"; (2) to attempt, again as far as possible, a rough assessment of the proportion of organic and functional elements in the pain; (3) for the vast majority, to *reassure without treatment*; (4) to treat by physical medicine, corset or plaster jacket, a selected small proportion; and (5) to operate (spinal fusion) in the hand-picked residue.

It is the problem of reassurance which is the most important yet the least satisfactory, both to surgeon and patient. In the first place, one can only reassure an intelligent, decent, and sensible patient. Most of the patients to whom these adjectives can be applied have already been reassured by the first two doctors they have seen—that is, the general practitioner and the first health service consultant on the "periphery." This means that the teaching hospitals, as final courts of appeal, accumulate an astonishing number of patients of a type impossible to reassure, and yet who have already received one or more complete courses of physical treatment at their local hospitals.

In the second place, the process of attempting to reassure a patient by sympathetic explanation is extremely exhausting for a conscientious consultant when he knows he is talking to a "brick wall." It takes a much longer time, and satisfies this type of patient less, than to send them off for a six weeks' course of quackery in the 30 seconds it takes to sign a chit. Unlike the bottle of coloured water, the cost to the State of placebo physiotherapy is fantastic. Many of these patients have the impertinence to say that "nothing has been done" for them after *x*-ray examinations (often in two or three hospitals), interviews with several consultants, and the fitting of a corset, when to get the same service over the same period of time in private practice would easily add up to £50.

If orthopaedic surgeons were to relax their strict grip on *ad lib.* physiotherapy, within as short a time as three years the backache problem would become totally unmanageable. Physical medicine can never *cure* low backache, and if pampered the first time the majority of these patients will be back again with another attack of chronic lumbago a year or so later. If given physical medicine the first time, it becomes humanly impossible to deny a second course if the patient is convinced, *post hoc propter hoc*, that the first course "cured" her. There is hope that in the near future pain arising in "collagen degeneration" may be brought

under control, which research is common ground for rheumatology, physical medicine, and orthopaedic surgery. Until this happy day dawns I believe that the majority of orthopaedic surgeons show a very highly developed sense of perspective in regard to pain and the public purse.—I am, etc.,

Manchester, 3. JOHN CHARNLEY.

Anaemia of Newborn Following Anterior Placenta Praevia

SIR,—We were interested to read the article on this subject by Drs. N. R. Butler and J. D. Martin (*Journal*, December 18, 1954, p. 1455). They have performed a useful service in drawing attention again to the risk of blood loss from the foetal circulation if the placenta is damaged during caesarean section—although their title hardly does justice to the urgency of the post-haemorrhagic shock which may occur in the affected babies. Your annotation (p. 1472) refers to our study of the same problem, reported elsewhere,[1] and rightly emphasizes the preventive aspect. We should like to report our further experience of this aspect.

During the period covered by our study the placenta had been encountered in the uterine incision on 20 occasions: 7 of the babies had lost sufficient blood to require a transfusion, and one of them actually died at the age of 3½ hours from post-haemorrhagic shock. During the subsequent 20 months meticulous attention has been paid to the details of the delivery in all cases of this type, and the technique used has been that described in our earlier report and in your annotation. There have been 15 cases in which the placenta was encountered: none of the babies has required a blood transfusion, and in only 8 babies has it been considered necessary to carry out serial skin-prick haemoglobin estimations, after our preliminary assessment based on the relevant factors noted at the time of delivery. This experience confirms that the obstetrician can almost eliminate the hazard of foetal post-haemorrhagic shock in cases of anterior placenta praevia by using the recommended method of delivery.

But the hazard can never be completely eliminated, as illustrated by case 6 in our previous report, and we fully agree with Drs. Butler and Martin in their recommendation that appropriate arrangements should be made for dealing with such an emergency whenever caesarean section is performed in a case of placenta praevia. We are, however, surprised by their reliance on the haemoglobin level in the cord blood as an indication of the amount of blood lost. We have been astonished by the speed with which haemodilution does in fact occur in some of these babies, as judged by the fall in the haemoglobin concentration in skin-prick blood during the first few hours of life, but it seems a little much to expect a significant fall immediately, or at the most within a few minutes of the haemorrhage, particularly if the estimations are made by a method whose margin of error is as great as that of the Haldane technique. It seems wiser to make an estimation as soon as possible after delivery and regard this as a base-line; subsequent serial estimations can then give an idea of the rate of haemodilution. We have found skin-prick blood satisfactory for this purpose if the foot is well warmed and a deep "prick" is made with a scalpel blade, and the M.R.C. "grey-wedge" photometer is used for making the estimations.—We are, etc.,

G. A. NELIGAN.
J. K. RUSSELL.

Newcastle-upon-Tyne.

REFERENCE

1 *J. Obstet. Gynaec. Brit. Emp.*, 1954, 61, 206.

Pure Red-cell Anaemia

SIR,—May I be allowed to make the following remarks on the interesting article of Drs. J. N. Marshall Chalmers and K. Boheimer (*Journal*, December 25, 1954, p. 1514)? The now popular name "pure red-cell anaemia" comprises several, at least three, different morbid entities. The disorder which I described in 1927[1] as erythrophthisis, and in 1952[2] as erythronophthisis, is acute or subacute, fatal or self-limited, non-haemolytic, and does not respond to any known treatment except blood transfusions. It is identical with one example of "aplastic anaemia" described previously by Kaznelson.[3] The second disorder, which Cathie[4] aptly calls erythrogenesis imperfecta and which was previously known as the Blackfan–Diamond type of hypoplastic anaemia, is congenital, has often in the early stages signs of increased haemolysis, shows some improvement with A.C.T.H. therapy and sometimes spontaneous amelioration after years of duration. A disturbance of tryptophan metabolism with excretion of anthranilic acid in the urine has been claimed, but this I could not confirm in one examined case. The third disorder is that described by Chalmers and Boheimer. The association of two such rare diseases as thymic tumour and pure red-cell anaemia is certainly not fortuitous. While the two other forms of pure red-cell anaemia occur only or mainly in children, this form seems to occur in adults only. It is of interest that the association of myasthenia gravis with thymic neoplasms (lympho-epithelioma), which is not uncommon in adults, has also not been observed in childhood. This form of anaemia may show recovery or remission after thymectomy, splenectomy, and A.C.T.H. therapy, or it may progress to typical aplastic anaemia, as in the case observed by Dr. Brewer.[5] Finally, we have to bear in mind that an aregenerative anaemia involving only the red blood corpuscles may occasionally develop as the result of Rh iso-immunization. This I observed in a pair of twins, who, in addition to signs of increased haemolysis, such as hyperbilirubinaemia without bilirubinuria and increased amounts of faecal pigments, had very low reticulocyte counts and a decreased number of nucleated red cells in the marrow. The nucleated red cells are very scanty or absent in the bone marrow in all above-mentioned disorders, and such as seen are of the most mature type. Only in the first weeks of life in erythrogenesis imperfecta normoblasts may be slightly increased in number.—I am, etc.,

Birmingham, 16. H. S. BAAR.

REFERENCES

1 *Folia haemat. (Lpz.)*, 1927, 35, 111.
2 *Acta haemat. (Basel)*, 1952, 7, 17.
3 *Verh. disch. Ges. inn. Med.*, 1922, 34, 557.
4 *Arch. Dis. Childh.*, 1950, 25, 209, 313.
5 Personal communication, 1954.

Tuberculous Patients in General Hospitals

SIR,—I wish to give my wholehearted support to the call of Dr. Arnold B. Cowan (*Journal*, November 20, p. 1227) for the medical profession to rise as a body against allowing patients suffering from pulmonary tuberculosis to be admitted into the wards of general hospitals. Until a few years ago we built sanatoria specially designed for the treatment of tuberculosis on what was regarded as the most healthful site, on the sound and established knowledge of the disease, and no patient with tuberculosis was allowed to be admitted into the wards of general hospitals, and if during treatment for any other condition any patient was found to have developed pulmonary tuberculosis he was immediately sent out. There was good reason for this. The general hospitals were not constructed to treat tuberculosis with safest and best methods, and student nurses are at the most susceptible age to contract tuberculosis. The exacting nature of their closed institution work for the sick, the strains to which they are subjected on duty, and the ever-increasing diminution of their leisure and rest brought about by the need for preparation for examinations constantly elaborated by the ever-increasing demands of the specialists, render them highly sensitive to tuberculosis. The Prophit Tuberculosis Survey[1] showed instances of nurses who had contracted the disease and had been kept on duty in spite of clinical and radiographic evidence of progressive disease—indeed, until, on leave, the parents detected the obvious decline.

We are short of nurses, more particularly in tuberculosis and mental institutions. The authorities have offered increased salaries and other inducements; they have repeatedly announced their needs in the public press, and have used all the methods of inducement which propaganda

offers, but the girls will not respond. The explanation is obvious to every unbiased layman. Therefore these demands for enforced labour in these institutions during the training will obviously result in less girls taking up nursing. Why should girls seek posts demanding self-sacrifice and self-denial when there are plenty of posts which have conditions which permit the commendable self-indulgence of the Welfare State?

It has been abundantly shown that improvements in housing and standard of living are far more important than quantity of medical care. Due to the former, the death rate from tuberculosis has been steadily and consistently falling from 80,000 to 8,000. There is no better place to treat tuberculosis than the home, and no one better fitted than the general practitioner to supervise it, particularly now that he ought to have available the effective drugs. Make the homes of the people fit for the general practitioner to treat the case at home and you will not only abolish the disease but lessen the enforcing factors which prevent girls becoming nurses.—I am, etc.,

Birmingham, 15. JAMES F. BRAILSFORD.

REFERENCE

1 Daniels, M., *et al.* (1948). *Tuberculosis in Young Adults: Report on the Prophit Tuberculosis Survey, 1935-44.* Lewis, London.

Premedication of Children for Tonsillectomy

SIR,—I am particularly interested in the correspondence following Dr. Christine M. Rendell's article (*Journal*, December 11, 1954, p. 1397) on the use of methylpentynol for premedication in children, as I myself have for some time been working on the same subject. I would suggest that the only satisfactory way of assessing a child's reactions to the experience of tonsillectomy is for a trained and independent observer to visit the child in its own home before and after its stay in hospital. It is obviously quite unreliable to ask the child while still in strange surroundings. The other way of recording a child's reactions is by means of a cinematograph record, such as was done by Robertson, of the Tavistock Clinic, in his film, "A Two-year-old Goes to Hospital." Both these methods have been carried out by me and are at present under preparation for publication.

I have been convinced that the elixir of "oblivon" as put up by Schering is of very great value for children. Admittedly no medicine will replace careful and tactful handling, but, having for years used atropine only as advocated by your correspondents, I have been very impressed by the ease of handling and induction since I have used oblivon. This shows very well in my film record. The incidence of vomiting I frankly do not understand. I have not met a single incident in about 500 cases. The oblivon should be given one hour before induction and followed by the atropine half an hour later. The child does not then mind this insult to its feelings. To those cases which arrive in the induction room still not fully sedated I then give a small "sleep dose" of intravenous thiopentone, quite a safe and easy procedure in a quiet and peaceful child, and not followed by any unsafe respiratory depression. But I hope your correspondents will see my film when it is ready. This will be more convincing than any letter.—I am, etc.,

Worthing. F. R. GUSTERSON.

Mobile Physiotherapy Unit

SIR,—Dr. G. A. Powell-Tuck's letter (*Journal*, December 11, 1954, p. 1422) rightly stresses the value of physiotherapy in the home. There is no doubt that many who need treatment are denied it because they cannot afford to pay private fees and cannot face the travelling and waiting involved in attending busy hospital departments.

A mobile physiotherapy unit was started 11 years ago to help these people, and the service is now available in about 20 areas. It could usefully be multiplied many times, but is restricted by lack of money. There is, I believe, only one unit financed by a local authority. The majority rely upon voluntary public subscriptions, contributory schemes, and help from existing charities. Where the need exists and enthusiasm can be aroused, advice upon starting a unit is to be had from the Mobile Physiotherapy Services Association of 12, South Audley Street, London, W.1.—I am, etc.,

Redhill. HENRY S. ATKINSON,
Chairman,
East Surrey Mobile Physiotherapy Unit.

Intussusception in the Newborn

SIR,—I have read the article by Mr. Stewart Feggetter (*Journal*, December 4, 1954, p. 1335) about a case of intussusception in a newborn baby. Recently I have sent an article to a Spanish medical review in which I refer to a case operated on by me of a strangulated inguinal hernia in a 15-day-old baby. Like Mr. Feggetter's case, my patient had melaena and I suspected an intussusception. After a complete examination the diagnosis of strangulated inguinal hernia was clear. The operation was done with good results, and I think it worth emphasizing—in agreement with Mr. Feggetter—that the operative shock in the newborn is frequently well tolerated. I agree with the author that nurses experienced in this type of work are very important. In my case I had aiding me an English nurse who specialized in babies' cases, and her work was perfect.—I am, etc.,

Rio Tinto, Spain. T. DE VEGA RUIZ.

Fatal Rupture of Retro-pharyngo-oesophageal Abscess

SIR,—In reference to the report (*Journal*, December 25, 1954, p. 1530) of a previously healthy girl, aged 10, dying as the result of fatal rupture of a retro-pharyngo-oesophageal abscess, is it not possible that if no antibiotics had been given the natural resistance of the girl would have localized the infection, an abscess would have been discernible, incised, and recovery taken place? In a report of an address given by Sir Heneage Ogilvie entitled "The Future of Surgery" (*Journal*, December 18, p. 1435) he gives a profound warning in reference to the dangers of the indiscriminate use of the antibiotics.

Is it not significant that no record of a case resembling the one reported could be found?—I am, etc.,

Hurstpierpoint. KENNETH EDRED PEMBREY.

Carcinogens in Cigarette Smoke

SIR,—Professor R. D. Passey (*Journal*, December 18, 1954, p. 1485) states that it is striking that "the increase of cigarette smoking has not been matched by increase in the incidence of carcinoma of lip, tongue, larynx, or buccal cavity," and that "a reduction in these sites, which, of course, are those exposed to the greatest concentration of smoke," is strange. At least three factors are concerned in carcinogenesis—namely, the concentration of particles in intimate contact with the surface concerned, the period of the latter's exposure, and its sensitivity to the particular carcinogen. Thus the mule-spinner develops scrotal carcinoma due to the prolonged contact of his oil-soaked garments on a particularly sensitive epithelial surface, and the process of carcinogenesis due to aromatic amines in bladder carcinoma takes some 15 to 20 years to develop.[1] I would suggest that these factors in carcinogenesis are more marked in the respiratory tract distal to the trachea than in the other sites described.

Concentration.—Smoke taken into the mouth is admittedly present in considerable concentration in the air, but, as it is mostly expelled at the next expiration, relatively few particles pass into the fluid lining the buccal cavity. In the respiratory tract, particularly in those inhaling deeply, it will be less rapidly cleared, and particles will tend to be retained, and reach high concentration in the mucus layer lining the tract. *Sensitivity.*—The effect of cigarette smoke on the bristling eyebrows of men and the hair-covered skins of mice, which have the function of protection as their main office, is in no way comparable to the effect of that smoke on the sensitive, delicate "naked" respiratory mucosa. Further, the specific sensitivity of two mucosae, say buccal and bronchial, to a given carcinogen could well vary, particularly when histological differences are taken into account. *Period of Exposure.*—Normally, the particle-collecting respiratory

mucus layer is passed by ciliary action, or coughing, to the larynx and thence to the pharynx to be swallowed. A heavy smoker will tend to chronic bronchitis, and, although the frequent coughing will tend to clear the trachea and proximal parts of the main bronchi, reducing their exposure time, the deleterious effects on the mucus-propelling ciliary action will result in a raised active exposure time. The cilia, further, are more abundant in the smaller bronchioles than in the larger ones and the bronchi, and predilection of carcinoma for the latter may well be due to the relative stasis of the carcinogen-bearing mucus layer at these sites.

Relative to these factors, the rapid passage to the pharynx of the particles passing into the profusely secreted and frequently swallowed buccal fluids leaves little opportunity for prolonged or concentrated buccal carcinogenic activity. There is probably some hold-up of these buccal and the returned respiratory carcinogenic particles at the crico-pharyngeal sphincter between the pharynx and oesophagus (the hypopharynx), and it is interesting to note that the incidence of carcinoma in this site has about doubled in the last decade.

Professor Passey's second point, that of the decrease of carcinoma at various sites, is not easily explained—the decrease being absolute, not relative. An awareness of the dangers of introducing carcinogens such as clay-pipes and tar-coated thread into the mouth is now widespread, and, with improvement in dental conservation and prosthetic treatment, the chronic irritations of the jagged tooth and ill-fitting dental plate have decreased. Further, and most important, with a considerable decrease of incidence of syphilis the occurrence of advanced syphilitic leucoplakia with its precancerous and malignant stages is now rare. These factors are not pertinent to the decrease in laryngeal carcinoma. This decrease, however, is not outstanding, the figures[2] for male incidence in the years 1943, 1947, 1951, and 1953 being 827, 769, 805, and 737. This may be explained by assuming that the respiratory tract is, in some unspecified way, varyingly sensitive to carcinogens; then individuals in the high sensitivity group are more likely to develop the bronchogenic carcinoma in the 45 to 50 age group, and leave fewer to succumb in the 55 to 65 laryngeal carcinoma group.—I am, etc.,

Manchester, 13. MONTAGUE SEGAL.

REFERENCES

1 Case, R. A. M. (1953). *Brit. J. soc. Med.*, 7, 14.
2 *Registrar-General's Statistical Review of England and Wales*, 1953. Tables Part 1. Med., p. 16. H.M.S.O., London.

Ultra-violet Light Therapy in Paget's Disease

SIR,—It does not appear to be generally known that some cases of painful Paget's disease of bone derive a measure of relief from ultra-violet light therapy and that it is worth a trial when other measures have failed. It appears desirable to produce mild erythema and pigmentation of the skin and to irradiate not less than one-third of the total skin area. These patients are usually elderly, and the precautions or contraindications proper to their general condition must be followed. I regret that I do not remember the source of my original information in about 1938 so that due credit might be given.—I am, etc.,

Watford. H. RHYS DAVIES.

Operator and Anaesthetist

SIR,—May I reply to the letter of Mr. S. I. Freedman and his colleagues (*Journal*, December 11, 1954, p. 1416)? I have never said that thiopentone should not be used in the dental chair, only that the operator-anaesthetist might have difficulty in defending himself against a charge of negligence. Refinements of technique may make anaesthesia safer but cannot make it *absolutely* safe. We have to consider the law of averages. Sooner or later a complication such as laryngeal spasm or heart failure will occur, when I venture to predict that the complaints of the patient's surviving relations will be as nothing compared with the reproaches of the operator's conscience. What good purpose is served by taking useless risks?

The suggestion that the patient's doctor should be asked to certify that the patient is in a fit state of health for out-patient anaesthesia does not come from me but from a learned judge. The circumstances of the case (which is quoted in the article I referred to[1]) and our general experience show that the suggestion is not unreasonable and is in the patient's interest. Dental surgeons may disregard it if they choose, but only at their peril. I disagree with the writers' statement that contraindications to out-patient anaesthesia "are few and obvious," and also with the opinion expressed in the last sentence of their letter, which is contrary to general experience.—I am, etc.,

London, W.1. R. BLAIR GOULD.

REFERENCE

1 *Anaesthesia*, 1954, 9, 248.

Chlorpromazine

SIR,—There is a simple explanation for the occurrence of jaundice following prolonged *oral* administration of chlorpromazine, as reported by Dr. Bryan Eagles (*Journal*, January 1, p. 46). It has been shown[1] that chlorpromazine exerts a reversible depressant action on all forms of cellular life in a concentration of 1/400,000. Cells which possess a high degree of specialized activity, like the cells of the brain, are particularly susceptible to this action, which in part at least explains the drug's central action.

When given orally, the drug is presumably absorbed from the alimentary tract and passed into the general circulation by way of the liver, which is submitted to a relatively high concentration of the drug, before it is diluted by the general circulation. Next to those of the brain, the cells of the liver are as highly specialized and active as any in the body. It is not surprising, therefore, that after several weeks exposure to a dose of 75 mg. daily (approximately 1 mg. per kg. or 1/100,000 of gross body weight) signs of liver failure begin to appear. Even in these circumstances it is possible that some other factor depressing liver function must be present, for jaundice does not appear to be a common complication in psychiatric practice where high oral dosage over prolonged periods appears to be the rule. Nevertheless, it is a point worth bearing in mind, and the effects of continued high dosage on the livers of experimental animals needs further careful study.

In large single dosage the drug is relatively non-toxic. In one instance a patient made a complete recovery in three days after attempting suicide by taking 70 25-mg. tablets—a total dose of 1,750 mg.[2] This is more than can be claimed for barbiturates, prolonged oral administration of which in their early days was reported to cause serious liver damage and jaundice.—I am, etc.,

London, S.E.11. D. A. BUXTON HOPKIN.

REFERENCES

1 Decourt, Ph. (1953). *Thérapie*, 8, 846.
2 Gosset, J. Personal communication.

Herpes Zoster Treated with Vitamin B_{12}

SIR,—In response to inquiries which have reached me from time to time about my letter (*Journal*, April 22, 1950, p. 959) on the use of vitamin B_{12} in herpes zoster, may I request the courtesy of your columns for further comment? In that letter I described the extraordinarily rapid results I had obtained in the treatment of shingles by giving injections on the first, second, and fourth days respectively of 50 micrograms of B_{12} each, and the avoidance in most cases of post-herpetic neuralgia. Treatment and dosage schedules were, unavoidably in general practice, empirical.

A consulting dermatologist friend of mine was kind enough to inform me some time ago that he had been able to diagnose a severely ill child, admitted to hospital on account of meningism, as a case of herpes zoster involving the ninth cranial nerve and therefore presenting the typical eruption of shingles on the soft palate. He gave B_{12}, and to everyone's joy and satisfaction the child was well within four days. Other doctors have also taken the trouble to let me know of their experiences, and to them I wish to extend my sincere thanks. The general consensus of opinion would seem to be that this treatment is of great value. Since then I have tried variations in frequency and dosage

of the injections, but my impression is that the original schedule suits the majority of cases, and I was unable to observe any benefit from doubling the dose. Leitch[1] has recently treated cases by a single injection of 1,000 micrograms with very good results, and I am anxious to try this.

I have, however, supplemented the treatment of my more severe cases by oral administration of B_{12}, giving some 150 micrograms q.d.s., and this has undoubtedly speeded up resolution, and in one particular case of an old lady, who had a herpes zoster ophthalmicus but who "could not stand the needle," I followed her first and only injection with oral administration of the vitamin, and she was completely well within eight days. Lastly, in view of the known but aetiologically uncertain connexion between herpes zoster and varicella, I have in the past two years been trying the effect of B_{12} in chicken-pox, in doses ranging from 150 micrograms t.d.s. to 200 q.d.s., depending on age, and results have been most gratifying. The rash has usually cleared within a week, there has been very little or no general malaise, and my main difficulty has not infrequently been to convince the mother that the rapidly disappearing rash has indeed been that of chicken-pox.—I am, etc.,

West Bromwich. K. E. JOLLES.

REFERENCE

[1] *Amer. Practit. (Philad.)*, 1953, 4, 800.

Footnote to History

SIR,—I was interested to read Dr. E. Ashworth Underwood's comment, in his review (*Journal*, January 1, p. 42) of Dr. William Brockbank's FitzPatrick Lectures, that neither he nor Dr. Brockbank had ever seen cupping performed with therapeutic intent. It fell to my lot to carry out both dry and wet cupping on several cases of nephritis when I was a house-physician in Glasgow in 1924. This fascinating, if archaic, manœuvre took place in the Royal Infirmary, but I rather think Dr. Underwood was a student at the Western Infirmary, which had presumably outgrown these foolish things. As for Manchester, I imagine cupping was abandoned when the Infirmary moved from Piccadilly to Oxford Road. It is unlikely that the vessels survived the flitting.—I am, etc.,

Sheffield, 10. W. A. RAMSAY.

Kaposi's Varicelliform Eruption

SIR,—The case reported by Dr. A. Fry (*Journal*, January 1, p. 28) appears to be wrongly named Kaposi's varicelliform eruption. Kaposi required the presence of eczema. An excellent paper written by Dr. G. I. Barrow (*Journal*, February 27, 1954, p. 482) covers practically all aspects of the subject. Reference to this paper, and indeed to many other papers, will reveal that Kaposi's varicelliform eruption arises on a basic eczema from infection by either herpes simplex virus or vaccinia. I suggest Dr. Fry's case is one of accidental vaccinia, the diagnosis suggested by the Home Office consultant who saw the patient.—I am, etc.,

Bradford, 8. ALLAN BIGHAM.

SIR,—Even four swallows do not of necessity make a summer, and Dr. A. Fry's patient (*Journal*, January 1, p. 28) with four lesions of accidental vaccinia was not, as he reports, a case of Kaposi's varicelliform eruption. M. Kaposi[1] described his eruption as a very alarming complication of eczema larvale infantum. He realized that the lesions were not varicella though they resembled it. They tended to be clustered most thickly on the eczematous areas, but smaller groups appeared on the previously intact skin in the neighbourhood. He had never seen any lesions appear elsewhere. Kaposi suggested that eczema herpetiform would perhaps be the most appropriate term, and the condition is accepted to-day as being a generalized herpes simplex.

It is true that vaccinia in an eczematous individual may be as widespread as Kaposi's eruption. In fact, generalized vaccinia in such individuals is regarded by some as another form of Kaposi's eruption—in this case eczema vaccinatum. The requirements for a diagnosis of Kaposi's varicelliform eruption are not, as Dr. Fry states, contact with a vaccinated person and the presence of vaccinia virus. They are an asthma-prurigo patient infected either with herpes simplex or with vaccinia virus.—I am, etc.,

London, W.1. BRIAN RUSSELL.

REFERENCE

[1] *Pathologie und Therapie der Haut Krankheiten*, 1887, 3rd ed., p. 483. Berlin.

Still Going Strong

SIR,—I was interested in Sir Cuthbert Sprawson's letter (*Journal*, December 4, 1954, p. 1359) reporting the great age of Dr. Abdul Karim, who is still practising his profession at the age of 98. This is possibly a record. However, in Prince Edward Island, Canada, still practising at the ripe old age of 97, is Dr. Roderick MacDonald still driving his car, and out in all weathers. In Canada Dr. MacDonald is most famous, and I had the pleasure of meeting him at a Medical Society meeting in Charlottetown, Prince Edward Island, some years ago.

During the war I remember meeting in Bassingham, Lincolnshire, a physician (the father of a friend of mine) who was also practising to a very ripe old age—his name, Dr. Osborne Johnson. Dr. Johnson, besides being a physician highly thought of in the countryside around Bassingham, was also something of a poet and an artist. I remember enjoying one of his poems, "Bayard's Leap," written at that time. Dr. Johnson, I understand, refused to have a telephone installed in his home. He believed if the patients wanted him they would come and get him. Perhaps Dr. Johnson had a point! It will be interesting to know of any other nonagenarians or centenarians still in practice.—I am, etc.,

Ayer, Mass., U.S.A. KENNETH I. E. MACLEOD.

Pre-operative Transhepatic Cholangiography

SIR,—I would be grateful for the courtesy of your columns for the following request for information. The Association of Surgeons at its meeting in Glasgow next April is discussing the subject of diagnostic procedures in obstructive jaundice. I have been asked to collect information on the position of pre-operative transhepatic cholangiography. This procedure has not been frequently carried out, and I would be grateful if any of your readers who have had experience of it would let me have a brief account of their results, including particularly any complications.—I am, etc.,

121, Harley Street, London, W.1. DAVID H. PATEY.

POINTS FROM LETTERS

Low Backache

Dr. HARRIS AVERY (London, S.W.16) writes: Dr. Leonard S. Calvert (*Journal*, December 18, 1954, p. 1488) does a service in reopening correspondence on the treatment of backache by manipulation. I do not think that the fault lies in the absence of efficient physical medicine departments. To my mind the whole attitude of the profession (and of our teaching) is faulty in this matter. Manipulation as a treatment is either ignored or misrepresented. I have a great respect for Mr. H. Osmond-Clarke as an orthopaedic surgeon and have often sought his opinion, but I was dismayed to read in your report of his lecture on cervical disk lesions (p. 1481): "Occasionally a manipulation *under anaesthesia* was a help" (the italics are mine). . . . Personally, I find the neck the easiest part of the spine to manipulate, since the muscle spasm can readily be overcome by steady, gentle manual traction. The neck should never, indeed need never, be manipulated under anaesthesia.

Medical Aspects of Boxing

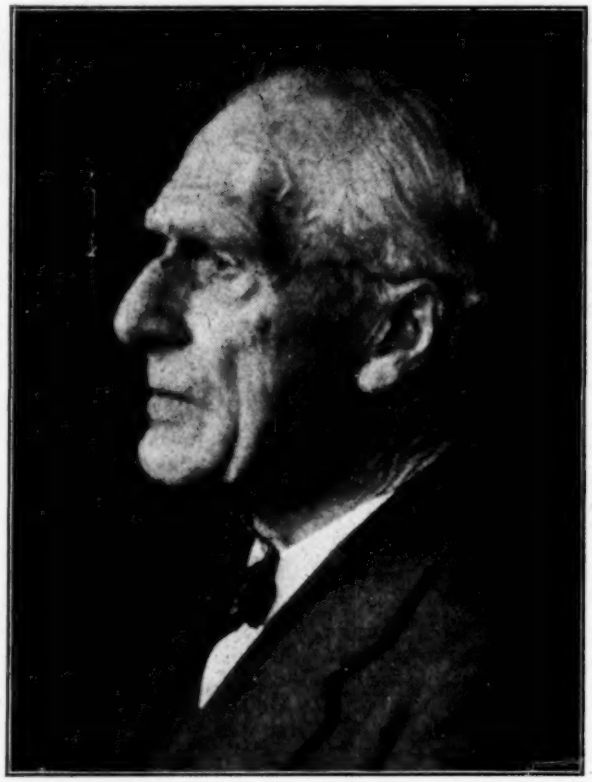
Mr. T. A. MASON (London, N.8) writes: With reference to the article by Drs. J. L. Blonstein and E. Clarke (*Journal*, December 25, 1954, p. 1523) and the leading article (p. 1535), I find it curious that no mention is made in text or bibliography of Dr. Jokl's book, *Medical Aspects of Boxing* (1941, Van Schaik, Pretoria). This is full of factual matter on the subject in question.

Obituary

Sir ARTHUR KEITH, M.D., LL.D., D.Sc. F.R.C.S., F.R.S.

We record with regret the death on January 8 of Sir Arthur Keith, whose anatomical and anthropological researches were world-renowned, and whose powers of exposition added lustre to an already highly distinguished scientific career. He was 88 years of age.

"To hear Keith," the late Lord Moynihan once said, "you would think he had never done anything—and he has re-made anatomy. The valley of dry bones, thanks to him, is full of living men." But Sir Arthur Keith was more than an anatomist; he was a physiologist, a pathologist, an anthropologist, above all a thinker. He interpreted to his own generation life in its origin and development, and no one could endow anatomy with more lively significance. In his teaching the long pathway of human history became suddenly illuminated. Like a detective reconstructing a crime from a broken lock and a finger-print, he was able from a few fossil remains to illustrate the evolutionary progress of man in a way which carried conviction with it. He made people feel that it must be so, that no other hypothesis was possible.



[J. R. Miller, Barnet

It was only necessary to glance at his facial contour to know that Keith came of East Scottish stock. To Aberdeen he was bound by many ties. He was born on a small farm near there, at Old Machar, in 1866, son of John Keith and Jessie Macpherson, who had ten children. One of Arthur's brothers, Robert Donald Keith, was principal of the King Edward VII Medical School at Singapore at the time of his death in 1918. Arthur Keith left school for a time at 13, but his father decided that his education must be continued. After a short time at Gordon's College he went on to study medicine at Marischal College, the founder of which, in 1593, was a Keith. He graduated M.B. in 1888, and proceeded M.D. of Aberdeen, with the highest honours, in 1894. In later life he was made LL.D. of his old university, and nearly fifty years after entering it as a student he was elected and remained three years its rector.

After graduation Keith went into general practice in Mansfield for a short time, and then, answering the call of adventure, went out to Siam as medical officer to a gold mine. Here, until the mine failed, he studied the anatomy of the Catarrhine monkeys, and on his return home he was awarded the Struthers medal and anatomy prize at Aberdeen University for his written account of his observations. After further study at University College, London, and at Leipzig, he eventually got the start he needed in a career of scientific achievement when he was appointed senior demonstrator of anatomy at the London Hospital in 1896. He soon became recognized as an outstanding teacher, and from 1899 to 1902 he was secretary of the Anatomical Society of Great Britain. It was at this time that he wrote his well-known work, *Human Embryology and Morphology*, which has since passed into several editions. At the London Hospital Medical School he took as his guiding principle that the men he taught would do their ward work all the better if they knew something of the history of the human body. To him the criterion for the admission of new matter into the teaching of morphology was its historic value—that is to say, the light which it threw on the origin and nature of the human body. He insisted throughout his teaching career on the close link between anatomical teaching and clinical experience. It was while Keith was at the London that he and Dr. Martin Flack discovered the sinu-atrial node (often called the pacemaker of the heart) at the junction of the superior vena cava with the sulcus terminalis of the right auricle.

In 1908 Arthur Keith, who had been a Fellow of the Royal College of Surgeons already for fourteen years, became Hunterian professor and conservator of the museum, a position he held for a quarter of a century. When on a May morning in 1941 only the ruins of the museum remained after a night of enemy bombing, the thought uppermost in many minds was the tragedy that this must mean to Keith, although by that time he had been retired from Lincoln's Inn Fields for eight years. Many men helped to make that museum the priceless thing it was, but Keith was chief among them. His knowledge and imagination and devotion made it the greatest collection in the world, illustrating the phenomena of life in both health and disease. He made it far more than a museum: he gave it character, significance, and unity. It became a great centre of instruction, a thesaurus of reference, a museum of history. Apart from the value of the specimens, which was beyond compare, it had for Keith—at least the nucleus of it—the sacredness of a legacy from John Hunter, like himself a Scotsman, a master of anatomy, a philosophic inquirer, a teacher, dissector, and experimenter. Hunter never had a more ardent disciple: nothing delighted Keith more than to show how some new advance had been foreshadowed in Hunter's teaching.

In 1932, after a severe breakdown in health from which he made a slow recovery, he resigned his work at the

College in Lincoln's Inn Fields to become Master of the Buckston Browne research farm at Downe, in Kent. Six years before, as president of the British Association, he had made an appeal for the preservation of Down House as a memorial to Darwin, who lived there for forty years, and Mr. (later Sir) Buckston Browne came forward and established a fund for that purpose. The research farm was added later. It fell to Keith to declare Down House open to the public. He spoke of the profound impression made upon him on first visiting that place: "I obtained a background for a mental picture in which the living Darwin moved, experimented, and thought. Science cannot be separated from personality. In making this place a national heritage we are acknowledging that sentiment has a place in science—not in the work of the laboratory, but in the heart of the worker." Here in his later years he found a grateful task in supervising the work of the young surgeons who studied on the research farm. Speaking of his work as Master of the Buckston Browne research farm, he said: "It brings to my door the keenest and most enterprising minds to be found in the surgical youth of the rising generation. It gives me young and congenial company." Despite his years he remained remarkably active, and when going to inspect the farm from his house, "Homefield," he still had a robust Scots look, wearing a tam-o'-shanter and a cape. Only the day before he died he was pruning his fruit trees.

Keith's first published work was his *Introduction to the Study of Anthropoid Apes*, published in 1896. Then came *Human Embryology and Morphology*, already mentioned. In the preface to the fifth edition of that work he said that successful textbooks were particularly exposed to the danger of overgrowth. Just as dominant stocks of animals have been hurried to extinction in past geological ages because their bodies became so big as to be unwieldy, so most valuable and prosperous textbooks have been killed by overgrowth. But Keith was as adept with the blue pencil as with the pen. Another work of his early years was his editing of Hughes's *Practical Anatomy*; he also assisted in Treves's *Surgical Applied Anatomy*. Later works of his bear such titles as *Ancient Types of Man, The Human Body, Nationality and Race, The Religion of a Darwinist*, and *Concerning Man's Origin*. For a succinct account of the evolution of man, including the lessons to be learned from the fossil skulls found in various parts of the world, Keith's article in the fourteenth edition of the *Encyclopaedia Britannica* cannot be bettered.* He was for many years an occasional and much-valued contributor of signed and unsigned articles and reviews to this *Journal*. Nothing dull ever came from his pen: he seemed to enjoy writing; at any rate there was no hint of effort, though the MS. showed evidence of careful revision. The only task he declined for the *British Medical Journal* was to write about the Hunterian Museum after its bombardment, pleading (with truth) heart-sickness. Since the war he had published three books, including his long autobiography, and a book entitled *Darwin Revalued* will be published shortly. Both in his autobiography and in his *Antiquity of Man* Keith explained how he came to accept the Piltdown findings only with some critical hesitation; and in a letter to a friend (published in the *Sunday Times* of January 9), commenting on the recent discovery of the hoax, he wrote: "The story of the evolution of man, so far as we yet know it, has not in any way been damaged. . . . The tragedy of the situation is a loss of faith in the testimony of our fellow workers. That is how the Piltdown fraud strikes me."

His eminence in the world of anthropology and anatomy is attested by his presidency of the Royal Anthropological Institute, the British Association, and the Anatomical Society, his Fullerian Professorship of Physiology at the Royal Institution from 1917 to 1923, his secretaryship of the Royal Institution from 1922 to 1926, and his honorary doctorates of six universities. In 1913 he was elected a Fellow of the Royal Society and a member of the Société d'Anthropologie de Paris. He was knighted in 1913. Lady Keith (formerly Cecilia Gray, daughter of Tom Gray, the artist), whom he had married in 1899, died in 1934. There were no children of the marriage.

We are indebted to Sir GORDON GORDON-TAYLOR for the following appreciation:

> "Maecenas waits me on the Esquiline:
> Thither to-night go I. . . .
> And shall this dawn restore us, Virgil mine,
> To dawn? Beneath what sky?"

These lines from Kipling which refer to the passing of Horace so soon after the death of his patron and friend Maecenas have been ringing in my ears ever since I heard the news of the death of Arthur Keith which has followed so rapidly that of his most illustrious pupil in the world of anatomy: both Wood Jones and he were conservators of the Hunterian Museum in Lincoln's Inn Fields, and when considerations of age imposed their decree on the continuance of that office each was privileged to go on serving the Royal College of Surgeons of England in a diverse capacity till "the end of the road," and each man died, as he would have wished, in harness and full of years. It is less than two months since we read Arthur Keith's charming obituary notice of "Freddy" Wood Jones in the *Annals* of the College of Surgeons, and the admiration and affection existent between the two will be self-evident to those who did not know them intimately from the terminal paragraph in Keith's notice, which I venture to quote and which is in fact a letter from Wood Jones on Keith's birthday, February 5, 1949:

> "This is to carry from Gertrude and from me all good wishes, and all hopes that these good wishes may be repeated for many years to come. It is a long time ago (1897) that as a first-year student I sneaked into, and was fascinated by, a lecture you gave on a boy with an extra pair of legs (a parasitic foetus) who was on show in Wonderland. That's more than fifty years ago. I have a fancy that in parental fashion you still look on me as a wayward youngster [which was quite true, A. K.]—(you do, don't you?): but I would have you know that I am over 70 now and almost grown up. Seventy or 20 it is no matter. I loved and admired you then and I still do and will. And Gertrude and I send our love to you."

I hesitated before acceding to the request that I would contribute something on Arthur Keith towards the columns of the *British Medical Journal*, for I feel at all times abysmally humble in the presence of Fellows of the Royal Society and deeply self-conscious of any attempt of mine at appraisal of scientific worth and stature, and it is only my loyalty to the memory of Arthur Keith that makes me take up my pen. His roots were grounded in the Turriff–Huntly area of the north-east of Scotland, where his father farmed and whence sprang my own maternal forebears; he trod the same academic groves that I was to tread more than a decade later; he was cradled in the basic sciences and in the clinical subjects by men under whom I myself was trained or who were friends of my family—then like "Jimmy" Trail and Alleyne Nicholson, and Japp, and "Johnnie" Struthers, who first stirred Keith's interest in anatomy; Smith Shand

in medicine and Alec Ogston in surgery, to whom he proudly refers in that delightful book, *The Menders of the Maimed;* Stephenson—nicknamed "Howdy"—the obstetrician; and that great old clinical teacher, Angus Fraser. But best of all he breathed the air of the Granite City and learned to work as perhaps the Aberdeen student alone can or could work in the last quarter of the nineteenth century.

Arthur Keith's connexion with the London Hospital round the beginning of the century brought him in contact with a coterie of men from the north-east of Scotland—William Bulloch, J. J. R. Macleod, and Henry Souttar had at least a temporary lodgment in old Aberdeen. I first came in touch with him personally over fifty years ago, when with characteristic generosity he lent Victor Bonney and myself all his manuscript notes and drawings dealing with the myology of the Primates, which represented his work in the Eastern Archipelago in his early postgraduate years. Although I never enjoyed the privilege of that intimate friendship with Keith that I had with Peter Thompson and F. G. Parsons, I used to see him at meetings of the Anatomical Society up to the outbreak of the first great war. Those were the days of Dan Cunningham, father of the distinguished Admiral and General, and George Thane; of Arthur Robinson, Howden, Hepburn, Waterston; of Paterson, of Liverpool; Ernest Frazer and Dixon, of Dublin; and Duckworth, of Cambridge. Fawcett made his three-monthly contributions on the ossification of still one more cranial bone; Lockwood still looked in occasionally; and there was always the stupendous frame of William Wright radiating happiness and good nature. Symington was busy cutting the body in sections, and Grafton Elliot Smith working on the morphology of the cerebrum, and the Hunterian Museum is enriched by his industry. Christopher Addison was still teaching anatomy, although already imping his wings for his brilliant flight into the empyrean of politics. War had not yet translated Auckland Geddes to ministries and an embassy. And Bertram Windle was still writing on monsters and abnormalities. Perhaps at no period was there such a galaxy of stars in the anatomical firmament, and from this group Keith was elected in 1908 to be conservator in Lincoln's Inn Fields.

In the days of his conservatorship the Museum which had for a hundred years been a lodestone for the surgeon and savant as well as for the curious became a Mecca as never before: specimens of every kind poured in, and when the Museum suffered from Hun bombardment there were some quarter of a million specimens, mounted or in the stores.

Keith's breadth of vision was enormous: although in later life he became more and more interested in anthropological problems, he always retained his interest in embryology as well as anatomico-pathological problems. I still possess a letter which he wrote me in the beginning of April, 1918, acknowledging the safe arrival of a specimen of a gunshot wound of a Meckel's diverticulum, which I resected during the terminal phase of the Fifth Army retreat in March, 1918, saying that its safe arrival during such a period of chaos was a "harbinger of the favourable tide of fortune which was shortly to roll in our direction." His Scottish industry was unflagging, and more and more he became involved in anthropological problems. He wrote books, brought out new editions; and he extended his hand to all.

The exigencies of war and the remoteness of his ivory tower at Downe curtailed the frequency of our meetings, but he was much loved by those who worked at the farm. But the vision still remains with me of the tall, active figure flitting in his white coat along the corridors and galleries of the College; and one can still hear the small, piping voice, the Scottish—though not the Aberdeen—accent, and the hurried sentences which were so attractive as they flowed from the lips of this kindly gentleman. In the words of Tacitus, writing of the Roman Agricola: "What we loved, what we admired in you endures, and will endure in the souls of men."

Professor A. J. E. CAVE writes: Keith's contributions to human anatomy embraced a wide range of original inquiries into such matters as visceral topography, the mechanism of respiration, the structure, function, and innervation of the bowel, the phylogenetic modifications of the axial skeleton, the growth of bone in health and disease, the effects of the upright posture upon the skeleton and soft parts, the growth, mensuration, and racial variations of the skull, cardiac physiology, and the development of the heart and great vessels. In investigating respiratory and alimentory function he unhesitatingly experimented upon himself in his determination to understand personally the working of the human machine. For Keith never dissociated any structure from its function, thereby proving himself a natural disciple of his fellow Scot, John Hunter, whose Museum he served with distinction as conservator for 25 years. Keith's principal anatomical achievements were perhaps his studies of the auricular musculature (1902–4), his verification (1905–6) of the Tawara cardiac conducting system, and his discovery (1906) with Martin Flack of the sinu-atrial (Keith-Flack) node. His numerous and sustained researches were directed to practical ends and designed to satisfy both anatomist and clinician; his early studies in physiology, teratology, primatology, and gross anatomy fruited in later years in his valuable and distinctive addresses, official lectures, and publications. His clinical sympathies were reflected in masterly studies of progeria, acromegaly, diaphyseal aclasis, pedal orthopaedics, and the nature and origin of hernia.

As anthropologist Keith became early on in his career a principal authority on questions touching ancient and modern man, his past and present racial origins, and his phylogeny, though herein his latter-day views found more public than professional acceptance. For years he examined and reported upon ancient human remains from Britain, Europe, Asia Minor, and elsewhere, and studied the racial composition and origin of the British people. In anthropological technique he invented a special craniometer, devised and promulgated the use of the sub-cerebral plane, and stressed the significance of cerebrospinal fluid streams in the interpretation of endocranial casts. He partook in the assessment of the status of *Pithecanthropus* and *Australopithecus* and of Rhodesian and Wadjak Man; described the Galilee neanderthaloid skull and (with T. D. McCown) elaborately monographed the Mount Carmel fossil Palestinians. In the original Piltdown controversy his anatomical experience put him initially in the right and, but for his militant Darwinism, might easily have bared the underlying truth. For overlong perhaps he maintained an undue antiquity for *Homo sapiens*, an attitude not unassociated with his unfortunate championship of the Galley Hill cranium and the Ipswich skeleton. Despite his modification of outlook in later years, he never wholly surrendered his belief in a direct common ancestor for man and anthropoid ape. His numerous publications on ancient man gained a wide popularity, but his later pronouncements in the field of social anthropology, wherein he abandoned accepted anthropological terminology, failed to command a comparable respect.

H. W. B. writes about Sir Arthur Keith when he was head of the department of anatomy at the London Hospital: In his early 40's Keith had a face of singular charm, with a quality of ascetic beauty, blue eyes, an aquiline nose and a forehead surmounted by a wave of fair curly hair, and furrowed by lines which gave him an air of rather anxious perplexity. He had an engaging manner with a hint of diffidence. His voice was gentle, with at times a pleading lilt in it, and his whole personality would seem to have belied the bitterness which according to his autobiography clouded some of the controversies of his long life as a scientist. There always seemed something elusive about him, especially when he wished to escape from the importunities of the dissecting room to the quiet haven of his laboratory and research. He then wore a slightly guilty

air, and with a quaintly sidling gait seemed to be taking evasive action against his students, some of whom made it a point of honour to try to hinder his progress with questions about some real or imaginary difficulty relating to some part under dissection.

In his routine teaching his declared aim was to make anatomy of practical help to the G.P. in his daily work. To this end he devoted many of his lectures to clinical and surface anatomy, and his blackboard sketches, though of no artistic merit, usually clearly illustrated what pages of description would have left only vaguely complicated. In this facility he was perhaps equalled by that gifted teacher, Russell Howard, then his senior demonstrator, whose similarly effective diagrams were grotesquely crude, but whose knack of welding an elusive fact on to a reluctant mind with the white-hot flame of sarcasm was probably unique. Keith, as befitted a Scotsman, was given to occasional shafts of pawky humour. When bones were to be handed round his class, he was wont to remark that as with umbrellas, so with bones—no borrower ever thought it necessary to return them.

It fell out that his last lecture at the London was on bones. On his arrival the anatomy theatre was crowded with his students, who were determined to show their affection for him in no uncertain manner. All who could had secured a suitable bone from among those laid out for demonstration. By luck I had attached a fine specimen of the femur. At the end of a quiet and orderly lecture a pandemonium of cheers broke loose, and desks were pounded unmercifully by every available element of the human skeleton. In one segment at least of desk surface there was a deep acetabular-shaped depression, and a fine femoral head had lost its shape and its articular cartilage. Thus did Arthur Keith's students say farewell to a beloved teacher with the bones which were so much the powerful levers of his philosophy.

CLAUDE RUNDLE, O.B.E., M.D., D.P.H.

Dr. Claude Rundle, for many years medical superintendent of the Fazakerley Infectious Diseases Hospitals and Sanatorium, Liverpool, died suddenly at his home at West Looe, Cornwall, on December 24, 1954, at the age of 81. His parents belonged to Cornwall, but they lived for a time at Plymouth, where he was born on July 20, 1873. Other members of his family also achieved success in the careers of their choice: Engineer Rear-Admiral M. Rundle is his brother, and his sister, Miss Mary S. Rundle, who died in 1937, was the first secretary of the Royal College of Nursing, where she worked for nearly 18 years.

Claude Rundle was educated at Plymouth Corporation Grammar School and received his medical training at St. Mary's Hospital, London, qualifying M.R.C.S., L.R.C.P. in 1895. He graduated M.B. from London University in 1898, obtained the D.P.H. of the English Royal Colleges in 1901, and proceeded to the M.D. in 1904. His early appointments in the public health service included those of medical officer at the Gore Farm Convalescent Hospital, Dartford, senior assistant medical officer at the Grove Fever Hospital, Tooting, and medical superintendent at the Orchard Smallpox Hospital, Dartford—all under the old Metropolitan Asylums Board. In the great smallpox epidemic of 1901–2, which seriously affected London, he gave devoted service on hospital ships in the Thames estuary.

These experiences seemed to settle the course of Rundle's future career by creating in him an interest in the communicable diseases, and he was appointed medical superintendent of the two isolation hospitals at Fazakerley in 1906. The heavy incidence of the commoner infectious diseases as well as of tuberculosis in Liverpool had prompted the city council in 1898 to purchase a large estate of 118 acres at Fazakerley for hospital purposes, and when Rundle arrived to take up his new duties part of the scheme had been completed. His first important task was to deal with the organization and staffing of the main isolation hospital of 350 beds opened in the year of his appointment. During the next few years this hospital, together with the annexe built in 1901, became one of the most noted and efficient of the country's infectious diseases hospitals, and it was visited by doctors from all over the world. An additional unit was completed in 1917 under Rundle's guidance, and in 1920 a large sanatorium of 265 beds was opened on part of the estate, and he became its first medical superintendent, though retaining his responsibilities in connexion with infectious diseases. From 1920 until he retired in 1934 Rundle was in charge of all the units on the Fazakerley estate, amounting in total to more than 900 beds. He had been largely responsible for the planning and building of nearly half of this great system of hospitals and wholly, as they were completed, for their organization and administration over the long period of 28 years. *Si monumentum requiris, circumspice.*

Rundle held a commission in the Territorial Army from 1908 onwards and attained the rank of lieutenant-colonel in the R.A.M.C. during the first world war, commanding the Berrington War Hospital and No. 55 General Hospital in France. For his services he was appointed O.B.E. in 1919. A few years later he was appointed one of the deputy lieutenants for the county of Lancaster. He was for many years lecturer in infectious diseases in Liverpool University, and accepted responsibility for the revision of the third edition of Ker's *Manual of Fevers* (1927) and the third edition of Ker's *Infectious Diseases* (1929). He published many articles in the medical journals, some on bed isolation, of which in his work at Fazakerley he was a pioneer. In his late fifties he had two severe attacks of pneumonia, and as a result retired from the service of Liverpool corporation in 1934 rather sooner than was normally required. Even before his retirement he had built a small but charming house at West Looe in his own county of Cornwall. He leaves a widow, formerly Miss Florence M. Kerruish, and a daughter, Mrs. Patricia M. Valentine, both of whom are members of the medical profession.—W. M. F.

E. A. B. writes: I had the privilege of working under Dr. Claude Rundle for 14 years, and can recall his dignified military figure riding a bicycle from ward to ward on his daily rounds, and later driving an ambulance. This was essential, as the hospital was scattered over 118 acres of ground. Infectious diseases were very prevalent at this time, and frequent epidemics called for urgent action. Dr. Rundle was at his best dealing with these emergencies. His capacity for work was prodigious, and he set a high standard of work. He suffered neither fools nor slackers gladly but made allowances for human weaknesses. He was the pioneer of bed isolation methods of nursing and showed his implicit faith in them when after an operation for appendicitis he was nursed in a ward where various infectious diseases were treated under this régime. Dr. Rundle's equanimity was proof against all the strains and stresses that medical superintendents were in those days apt to come up against. His great wisdom and diplomacy poured oil on many troubled waters. From what I have written it may be thought that Dr. Rundle was difficult to work with: on the contrary he was a delightful and most approachable superior, whose personal kindness matched his profound knowledge, for he was always ready day or night

to give advice and help to his staff, medical or nursing. There are many to-day who remember him with affection and deep gratitude.

H. N. WEBBER, B.Chir., F.F.A. R.C.S.

We record with regret the death on December 24, 1954, of Dr. H. N. Webber in University College Hospital, which he served for over 20 years as honorary anaesthetist.

Harald Norris Webber was born in 1881 and was educated at Brighton College and at St. John's College, Cambridge, where he took the natural sciences tripos in 1903. He remained at Cambridge for another five years, doing research work with the late Dr. W. H. R. Rivers, who was lecturer on experimental psychology. Rivers was Croonian Lecturer of the Royal College of Physicians of London in 1906, and his lecture—on the influence of alcohol and other drugs on fatigue—was published in book form two years later. Webber never drank alcohol at all, and he was therefore an ideal subject for this investigation, and the lecture was based largely on experiments performed on him. Rivers and Webber collaborated further in the publication of papers on the action of caffeine and alcohol on the capacity for muscular work. In 1908 Webber entered University College Hospital and soon became dresser to Professor Arthur E. Barker, who had been the first man to introduce spinal analgesia to this country three years earlier. After qualifying in 1912 Webber became successively house-surgeon, house-physician, and resident medical officer at the West London Hospital. In the first world war he served in the R.A.M.C. from 1917 to 1920, attaining the rank of major. While with the Egyptian Expeditionary Force he developed a very severe attack of typhus, which left him in indifferent health for the rest of his life. On leaving the Army he was appointed assistant medical officer to the London Fever Hospital, and in 1922 he became resident medical officer at University College Hospital. During his term of office he had to administer anaesthetics in many emergencies, and this work led him to specialize as an anaesthetist. He had at one time intended to be a surgeon, but an accident resulting in a permanently stiff finger prevented this. In 1924 he was appointed anaesthetic registrar, and six months later he was elected to the honorary staff of University College Hospital. He was also elected to the staffs of St. Paul's Hospital and the Royal Chest Hospital, and he served for a time as anaesthetist to the Central London Throat, Nose, and Ear Hospital and the Royal Dental Hospital. He took the B.Chir. in 1928, and in 1948 he was elected one of the first Fellows of the newly established Faculty of Anaesthetists of the Royal College of Surgeons of England. He was a prominent member of the Section of Anaesthetics of the Royal Society of Medicine, being secretary from 1935 to 1937, president in 1940–1, and vice-president from 1941 to 1944.

Webber did not make many contributions to medical literature. His chief work was the textbook written in conjunction with his colleague, Dr. Felix S. Rood, entitled *Anaesthesia and Anaesthetics*, which appeared in 1930 and which for many years was the standard work on the subject. He also wrote the chapter on anaesthesia in Gwynne Williams's *Minor Surgery and Bandaging*. A few years after Boyle's original apparatus came out Webber introduced a modification which placed the ether and chloroform bottles in parallel instead of in series, thus preventing the passage of chloroform vapour into the ether bottle. This apparatus is still in use at University College Hospital and is preferred by many of Webber's colleagues to more modern apparatus. He was a sound teacher, always striving to follow the precept of his predecessor, J. T. Clover, that a man on leaving University College Hospital should be competent to give a safe anaesthetic without recourse to complicated apparatus.

Webber was reserved in character, but had a keen if rather sardonic sense of humour. His punctuality was proverbial, and on the rare occasions when he was late he would make a brief apology, and only when the afternoon's work was finished would he relax and smilingly give an account of the complications which had been encountered in the previous patient and which caused him to be late. He was wrapped up in the welfare of his hospital and devoted unsparingly his energies in working for it. Scrupulous in his care of patients, he always visited them before and after operation. During the last war he worked at University College Hospital in the Emergency Medical Service and seemed to be completely without fear, for, after being twice bombed out of his own house, he took a top-floor flat next door to the hospital. On retiring from the staff under the age limit in 1946 he became visiting medical officer to the Hostel of St. Luke in addition to carrying on his work there as honorary anaesthetist. He was a man of strong religious feelings, and gave to his patients there the same unsparing devotion he showed throughout his career right up to the time of his last illness. A year before he died he had to undergo a major abdominal operation which he met with characteristic fortitude. He married Madeleine Mary, daughter of Major J. J. Ryder, who survives him, and to whom we offer our deepest sympathy.

G. W. MILLER, D.S.O., M.B.

Dr. G. W. Miller, a general practitioner who was held in high regard in Dundee and beyond, died in a nursing-home at Dundee on January 5 at the age of 80. He had been ill for some months.

George Waterston Miller was born on July 27, 1874, the son of one of Dundee's most popular and respected practitioners, Dr. J. W. Miller, and he followed closely in his father's footsteps. He was educated at Dundee High School and at Edinburgh University and first graduated B.Sc. in 1895, winning Professor Geikie's medal in geology, before he turned to medicine. As a student, as well as in later life, he was popular with everyone. Fond of dancing, and a good singer, he was also a keen athlete, a first-class swimmer, a cross-country runner, and an excellent Rugby forward. He took the M.B., Ch.B. degrees in 1898 and then acted as resident physician under the late Sir Byrom Bramwell at Edinburgh Royal Infirmary. Returning to Dundee in the following year, he was resident physician at the Royal Infirmary for a year before settling in general practice. He continued his association with the Royal Infirmary, of which he was assistant physician from 1908 to 1919, and for almost the same period he rendered good service to St. Andrews University as assistant to the professor of medicine.

A keen Volunteer, Miller passed from the Dundee Rifles to the Black Watch in Edinburgh, where he was a member of the first Maxim gun team in Scotland, a team which also included E. C. (later Sir Eric) Geddes. He held a combatant commission as a Volunteer from 1891 to 1904, when he obtained a commission as a

medical officer. During the first world war, at the outbreak of which he held the rank of major in the R.A.M.C., T.A., he served in France with the 51st (Highland) Division from 1915 to 1919, being in command of a Highland field ambulance towards the end of the war. He was twice mentioned in dispatches and was awarded the D.S.O. in 1917 and the Croix de Guerre with silver star two years later. After the war he was in command of the 152nd Highland field ambulance from 1920 to 1924 and was A.D.M.S., with the rank of colonel, of the 51st (Highland) Division for four years from 1924. His services to the Volunteer movement were recognized by the award of the Territorial Decoration some years earlier.

An enthusiastic supporter of the St. Andrew's Ambulance Association, for which he worked as a lecturer and examiner for nearly fifty years, he was awarded the King's Medal with five bars in 1949. In 1908 he was appointed an honorary Associate of the Venerable Order of St. John of Jerusalem. He was a member of the British Medical Association for fifty-five years, and served on the Council for three periods, from 1922 to 1935, 1938 to 1940, and in 1943–4. He was also president of the Dundee Branch in 1922–3 and chairman of the Scottish Committee from 1927 to 1929. During the last war he acted as secretary of the Dundee Medical War Committee and was the local emergency officer. He was a good committee-man, his benevolent smile being typical of his kindly and honest disposition. His colleagues and patients will miss him sadly. He married Miss Maria L. Gilbert in 1901, and she, with their only daughter, survives him, his only son having predeceased him.

Dr. CHARLOTTE R. BROWN died in hospital at Banbury on January 1 at the age of 86. Charlotte Rhoda Brown was born in Tipperary, the daughter of Mr. William Hodgins, on October 18, 1868. Her early years were spent in her native country, and during her long life she never lost her interest in all forms of natural history, an interest bred in her as a girl through living in a house with a large garden in rural Ireland. She received her medical education at the London (Royal Free Hospital) School of Medicine for Women and took the Scottish triple qualification in 1895 and the Brussels M.D. in the following year. After holding several postgraduate appointments she was in general practice at Bradford until her marriage to the Rev. Richard E. Brown in 1901. She was the only woman medical practitioner in Bradford at the time, being one of the early band of women who qualified under difficult circumstances and against some opposition. She took an active part in the women's suffrage movement before the first world war, and any branch of work outside the home in which women played a part was of great interest to her. She was a member of the Medical Women's Federation for many years. In 1916 she joined the staff of the East Anglian Sanatorium at Nayland, and thenceforward specialized in the treatment of tuberculosis. In the following year she was appointed tuberculosis medical officer to the Essex County Council, and in 1919 she became medical superintendent of the Children's Hospital for Surgical Tuberculosis at High Beech in Epping Forest, where she remained until 1932, when she retired, combining the work of the post with that of a child welfare appointment. She and her husband then went to live at Welwyn Garden City, where they took a very real, although not a vocal, interest in the activities of the neighbourhood. Dr. Brown was a very lovable woman with a large circle of friends in Welwyn. She had a good sense of humour and would tell many stories against herself. She was excellent company, and her Irish background—the background of the Somerville and Ross "Irish R.M." stories—gave her an endless fund of anecdote and reminiscence.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **December 25** (No. 51) and corresponding week 1953.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1954					1953				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	15	2	4	0	1	15	0	7	0	
Dysentery	340	33	177	7		309	52	107	0	8
Encephalitis, acute	2	1		0		3	1	0	0	
Enteric fever:										
Typhoid	2	1	0	0	3	0	0	1	0	
Paratyphoid	5	1	1	0		1	0	0	0	
Food-poisoning	138	16		1		109	11		2	
Infective enteritis or diarrhoea under 2 years				8	12				10	10
Measles*	5,840	550	328	309	103	611	1	16	9	60
Meningococcal infection	28	2	16	2	1	21	3	15	0	
Ophthalmia neonatorum	27	6	7	0		30	2	2	0	
Pneumonia†	756	42	201	7		530	26	257	13	3
Poliomyelitis, acute:										
Paralytic	8	0	3	0		19	3	7	2	1
Non-paralytic	1	0				10	1			
Puerperal fever§	179	29	12	0		171	24	6	0	
Scarlet fever	673	52	108	31	20	949	50	212	26	28
Tuberculosis:										
Respiratory	493	56	102	15				109	17	
Non-respiratory	69	3	13	2				15	5	
Whooping-cough	1,256	89	110	19	7	1,424	56	252	39	52

DEATHS in Great Towns	1954					1953				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	1	0	0	0	0	0	0	0	0	0
Dysentery	0	0		0		0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	2	0	0	0	0	12	1	2	1	1
Influenza	56	3	4	0	0	12	0	2	0	0
Measles		0	0	0	0		0	0	0	0
Meningococcal infection	0	0	0				2	2		
Pneumonia	301	47	27	6	10	219	29	31	9	3
Poliomyelitis, acute	0	0			0	1	0			0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	85	13	20	1	2	80	9	27	2	1
Non-respiratory		1	0	0	0		1	2	0	0
Whooping-cough	2	1	0	0	0	3	1	0	0	0
Deaths 0–1 year	191	17	25	4	7	188	22	47	7	3
Deaths (excluding stillbirths)	5,626	746	599	87	126	4,541	637	641	88	104
LIVE BIRTHS	5,294	806	730	165	236	4,575	659	666	184	206
STILLBIRTHS	169	12	18			153	12	14		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

London's Health in 1954

According to a preliminary report by the County Medical Officer of Health, Dr. J. A. Scott, the 50,920 births gave a birth rate of 15.2 per 1,000. Deaths numbered 36,200. The provisional death rate was 10.9 per 1,000, the lowest ever recorded. The infant mortality rate was 22 per 1,000 live births, also a record low figure. The neonatal mortality rate was 16 per 1,000 live births, and compares with 16.1 in 1953 and 15.8 in 1952. The maternal mortality rate was 0.43 per 1,000 live and stillbirths. The incidence of epidemic diseases was low. After a rise in 1953, the infantile-diarrhoea death rate fell again and was the lowest recorded. 24 children under 2 died from this cause, compared with 65 in 1953; 8 years ago 269 died. The diminished mortality from this disease accounts for a large part of the drop in the general infant death rate.

Influenza

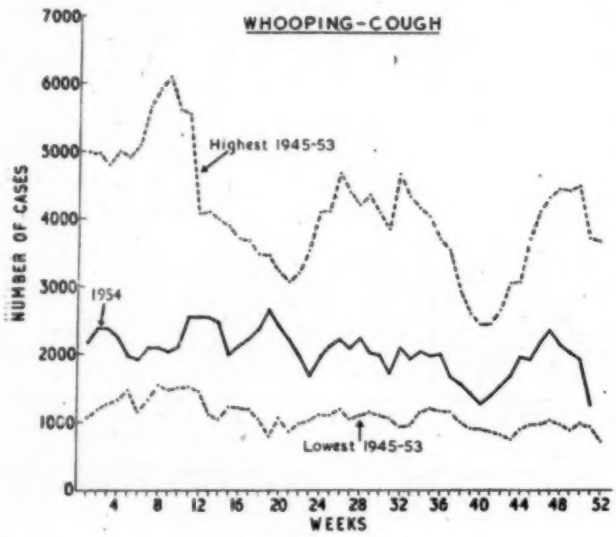
No reports have been received of further outbreaks of virus-B influenza in the northern and north-western regions or in Wales, and in these areas and in Scotland the infection is waning. In the north midlands and midlands fresh outbreaks continue to be reported in some areas not previously attacked, and additional outbreaks are apparently occurring in the south, south-west, east, and south-east. In London there are indefinite reports of a considerable amount of illness, much of which may be due to influenza. Clinically the disease on the whole remains mild. There is also some evidence of an increased incidence among adults.

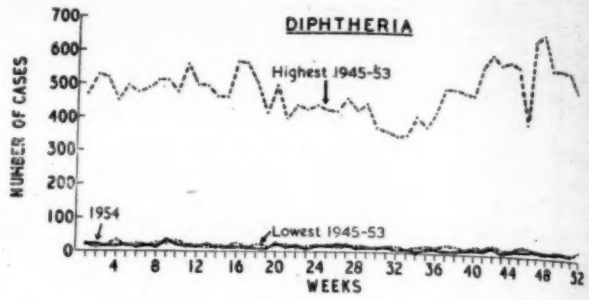
Week Ending January 1

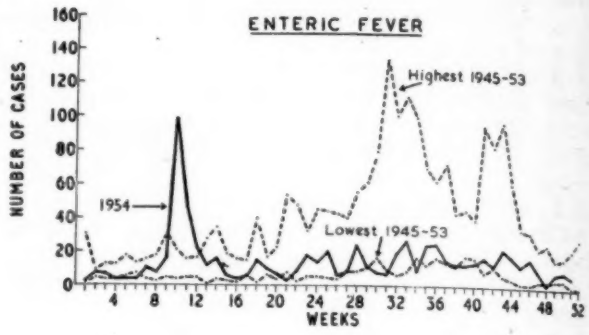
The notifications of infectious diseases in England and Wales during the week included: scarlet fever 707, whooping-cough 1,722, diphtheria 13, measles 8,320, acute pneumonia, 1,108, meningococcal infection 31, acute poliomyelitis 23, dysentery 340, paratyphoid fever 11, and typhoid fever 4.

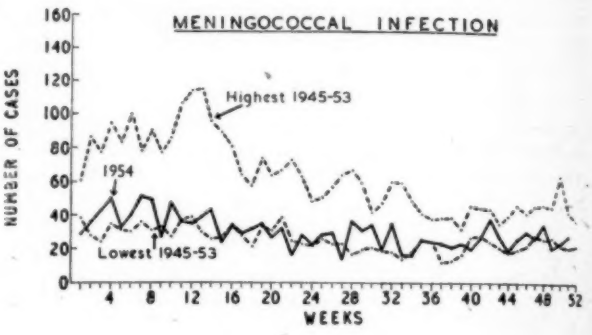
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1945–53 are shown thus - - - - - - -, the figures for 1954 thus ————. Except for the curves showing notifications in 1954, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

The notifications of infectious diseases in England and Wales declined during the week ending December 25, as is usual at Christmas time; the falls included 683 for measles, from 6,523 to 5,840; 577 for whooping-cough, from 1,833 to 1,256; and 125 for scarlet fever, from 798 to 673.

The largest declines in the incidence of measles were 480 in Lancashire, from 2,392 to 1,912, and 127 in Durham, from 433 to 306, and the largest increases were 161 in Yorkshire West Riding, from 397 to 558, 54 in Northumberland, from 39 to 93, and 49 in Staffordshire, from 173 to 222. A fall in the incidence of scarlet fever was recorded in most regions, but no large local variations were recorded. The largest falls in the incidence of whooping-cough were 100 in Lancashire, from 227 to 127; 68 in Staffordshire, from 96 to 28; and 42 in Durham, from 127 to 85. 15 cases of diphtheria were notified, being 3 fewer than in the preceding week. The chief feature of the returns of diphtheria was a fall from 9 to 2 in Lancashire.

Only 9 cases of acute poliomyelitis were notified, and this was the lowest number for any week for the past five and a half years. The notifications were 18 fewer for paralytic and 9 fewer for non-paralytic cases than in the preceding week. 2 cases were notified in Leeds C.B., the only area with multiple cases.

340 cases of dysentery were notified; this was the same total as in the preceding week. The largest returns were Lancashire 71 (Oldham C.B. 32); Norfolk 46 (Norwich C.B. 25); Yorkshire West Riding 41 (Sheffield C.B. 16); London 33; Warwickshire 20 (Birmingham C.B. 15).

56 deaths were attributed to influenza in the great towns, 10 fewer than in the preceding week.

Smallpox in France

The French Ministry of Health states that the port of Vannes in the Morbihan Department in Brittany has been declared infected with smallpox. Up to January 4, 13 cases, including two deaths, have occurred. Sanitary measures have been applied from that date to departing ships.

Quarterly Return for Eire

The birth rate for the September quarter of 1954 was 21.6 per 1,000 of the population, being 0.3 above the rate for the third quarter of 1953. The infant mortality rate was 30 per 1,000 births, and this was the lowest rate recorded in any quarter and 3 below that of the third quarter of 1953, the previous lowest level. The death rate was 10.5 per 1,000 of the population, being 0.8 above the rate for the September quarter of 1953 and 0.3 above the average of the five preceding third quarters. Deaths from the principal epidemic diseases included 39 from gastro-enteritis (under 2 years), 13 from influenza, 12 from whooping-cough, and 4 from acute poliomyelitis. Deaths from tuberculosis included 181 from respiratory and 45 from other forms. These deaths were, respectively, 8 above and 22 below the number registered in the preceding third quarter, and 142 and 67 fewer than the average of the third quarters of 1949–53.

Medical News

Sir Robert Robinson, O.M., F.R.S., was installed as president of the British Association on January 7. Sir Robert is Waynflete Professor of Chemistry at Oxford. He is perhaps best known to medical men for his wartime work on the structure of penicillin and for his more recent studies on the synthesis of steroids.

Pharmacology Laboratories at Leeds.—A new suite of research laboratories has been added to the Department of Pharmacology at the Leeds School of Medicine. This has been made possible by a grant of £10,000 provided by the Wellcome Trust. The new laboratories were opened on January 6 by Sir HENRY DALE, O.M., F.R.S., chairman of the Trust, during the recent meeting of the British Pharmacological Society in Leeds. The suite consists of five laboratories, office, store, and darkroom. The head of the department is Professor W. A. BAIN.

Clinical Research Fellowships.—The Medical Research Council invites applications for Fellowships in Clinical Research, tenable at centres in the United Kingdom during the academic year 1955–6. These Fellowships are open to suitably qualified medical graduates. The intention is to give each Fellow, as part of his training, an opportunity to study research methods in the basic subject most relevant to his particular clinical interest. Awards will be for one year in the first instance, and renewable annually up to a maximum of three years. Stipend will start at £850 per annum, rising by annual increments of £75 to £1,000 per annum, with superannuation provision in addition. Forms of application and further details may be obtained from the Secretary, Medical Research Council, 38, Old Queen Street, London, S.W.1, with whom applications should be lodged as soon as possible, and in any event not later than March 1.

Certificates for Meat Exports.—A certificate signed by a medical officer of health will in future be required to accompany all British exports of meat (and meat products) to Belgium. This is the result of a recent agreement between the two governments. Private certification of meat exports from Britain is quite common both to ensure customs clearance and to facilitate sales, but there are only two other official schemes—with the United States and Canada—and these date from about 1930. The reason for the new scheme is not any change in the nature of our meat trade, but recent domestic legislation in Belgium. The certificate declares that the meat has been derived from animals subjected to ante- and post-mortem examination, that it is wholesome and fit for human consumption, and that it has been handled only in a hygienic manner in this country. Specimen certificates may be obtained from the Ministry of Food, the Department of Health for Scotland, or from the Ministry of Agriculture, Belfast.

British Journal of Anaesthesia.—With its current issue, the *British Journal of Anaesthesia* becomes a monthly. Founded in 1923 as a quarterly, during the war and until 1950 the journal appeared only twice a year. In 1950, under the joint editorship of Dr. T. CECIL GRAY and Dr. E. FALKNER HILL, quarterly publication was resumed, and last year six issues were printed. To meet increased costs the subscription has been raised to £3 15s. inland (£4 4s. overseas).

Lepers in Revolt.—Newspapers report that on January 11 the 300 patients on Trinidad's leper island, Chacachacare, seized control of the island. They were protesting against the recall of their medical superintendent, Dr. MICHAEL CORCOS, for granting many of them Christmas leave on the mainland.

Italian Honour for Cerebral Palsy Worker.—Mrs. EIRENE COLLIS, head of the Cerebral Palsy Unit at Queen Mary's Hospital, Carshalton, was decorated last month with the Star of the Order of the Italian Republic. The occasion was the opening of the third congress of the Italian Society for Medical Gymnastics in Milan. The decoration was for her work in helping to establish cerebral palsy clinics in three Italian cities. Mrs. Collis is a pioneer in this field: it was at her instigation that in 1942 the London County Council established the Carshalton unit, claimed to be the first of its kind in Britain.

Chelsea Centre for Spastic Children.—An experimental day centre for the diagnosis and treatment of children under 5 years of age suffering from cerebral palsy will be opened shortly at Cheyne Hospital for Children, 61, Cheyne Walk, London, S.W.3. By arrangement with the London County Council educational facilities will also be provided. The centre will be administered by the Chelsea Hospital Management Committee, and will be closely associated with St. Stephen's Hospital, Fulham Road, the Westminster Hospital, and establishments dealing with the treatment of cerebral palsy. Parents living in south and west London wishing to apply for admission of a child should communicate with the Group Secretary, Chelsea Hospital Management Committee, St. Luke's Hospital, Sydney Street, Chelsea, S.W.3, through their family doctor.

William Gibson Scholarship.—The Royal Society of Medicine announces that the next award of the William Gibson Research Scholarship for medical women will be made in July. The scholarship, valued at about £200 a year, is tenable for two or occasionally three years. Candidates must be British subjects. Details may be obtained from the secretary, Royal Society of Medicine, 1, Wimpole Street, London, W.1.

Mr. B. W. Rycroft has been invited to become an honorary member of the Ophthalmological Society of South Africa.

COMING EVENTS

Radio and Television.—Tributes to Dr. ALBERT SCHWEITZER on the Light Programme at 8.30 a.m. and on the Home Service at 9.15 p.m. on Sunday, January 16. "Atoms for Export," a programme from the Radiochemical Centre, Amersham, on television at 9.45 p.m. on Tuesday, January 18.

Oxford Graduates' Medical Club.—Winter dinner at the Royal College of Surgeons, Lincoln's Inn Fields, on February 11, 7 for 7.30 p.m., under the chairmanship of Professor H. R. DEAN. Tickets (25s.) from Mr. SELWYN TAYLOR, 3, Roedean Crescent, Roehampton, London, S.W.15.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Friday, January 14

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., at Institute Lecture Theatre, open clinical demonstration by Dr. J. Smart and Dr. K. F. W. Hinson: Pulmonary Aspergillosis.

Saturday, January 15

KENT PAEDIATRIC AND CHILD HEALTH SOCIETY.—At Children's Department, Farnborough Hospital, Kent, 3 p.m., clinical meeting.

Monday, January 17

HUNTERIAN SOCIETY.—At Mansion House, 8.30 p.m., Hunterian Lecture by Professor J. Adams-Ray (Stockholm): Some Observations on a New Symptom-pallor in the Inflammation Syndrome.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. Macdonald Critchley: Parietal Symptomatology.

Tuesday, January 18

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Dr. Douglas McClean: Substances that Increase Tissue Permeability and their Relation to Infection and Fertilization.

ILFORD MEDICAL SOCIETY.—At King George Hospital, Ilford, 8.45 p.m., Dr. P. M. F. Bishop: Treatment of the Menopause. Members of the Stratford Division, B.M.A., are invited.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. M. S. Thomson: Tuberculosis Cutis.

OXFORD UNIVERSITY MEDICAL SOCIETY.—At Radcliffe Infirmary, 8.15 p.m., Dr. S. R. Gerber (Cleveland): Case of the Osteopath's Wife.

ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Goulstonian Lecture by Dr. G. M. Bull: The Uraemias.

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Theatre, 5 p.m., Dr. G. W. B. James: Neurosis in Gynaecology.

SOCIETY FOR THE STUDY OF ADDICTION.—At Medical Society of London, 8 p.m., Dr. M. M. Glatt: How a Treatment Centre for Alcohol Patients was Established at a State Mental Hospital and How it Works.

SOUTH-WEST LONDON MEDICAL SOCIETY.—At Bolingbroke Hospital, 8.30 p.m., Dr. F. E. Camps: Forensic Medicine and the Law.

Wednesday, January 19

EUGENICS SOCIETY.—At Royal Society, Burlington House, W., 5.30 p.m., Professor L. S. Penrose, F.R.S.: Genetics of Microcythaemia (Thalassaemia) (with a film).

HYPNOTHERAPY GROUP.—At Eastman Dental Hospital, Gray's Inn Road, W.C., 8 p.m., papers by Dr. W. Moodie, Dr. D. Stafford-Clark, Dr. G. F. Newbold, Dr. G. J. Ambrose, and Mr. E. Wookey.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. H. Haber: The Eosinophilic Granulomas of the Skin.

INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Dr. R. Thomson: Laboratory Aids to Diagnosis.

MIDDLESEX COUNTY MEDICAL SOCIETY.—At Ashford Hospital, 3 p.m., clinical cases; 4.30 p.m., Mr. F. G. Ward: Rehabilitation and Resettlement.

MIDLAND MEDICAL SOCIETY.—At Birmingham Medical Institute, 154, Great Charles Street, 8.15 p.m., Sir Stanford Cade: Progress in the Treatment of Cancer.

OXFORD UNIVERSITY.—At Radcliffe Infirmary, 5 p.m., Litchfield Lecture by Dr. E. J. M. Bowlby: Maternal Care and Mental Health.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW.—5 p.m., John Burns Lecture by Professor W. W. Mushin: Physiological Principles in the Care of the Unconscious Patient.

WILLESDEN GENERAL HOSPITAL MEDICAL SOCIETY.—At Department of Physical Medicine, 8.45 p.m., discussion: Some Common Dermatological Topics. Speaker, Dr. I. Muende.

Thursday, January 20

BRITISH INSTITUTE OF RADIOLOGY.—7.45 p.m., special general meeting, followed by ordinary meeting at which papers will be read as follows: Dr. A. H. E. Marshall, Some Actions of Hormones and Pharmacological Agents upon the Acute Skin Damage produced by *X* rays and Carcinogenic Hydrocarbons; Dr. L. E. Houghton, Dr. J. B. Walter, and Mr D. E. A. Jones, The Modification of *X*-ray Damage by Cortisone; Dr. K. Sicher, A Clinical Trial of A.C.T.H. in Radiotherapy.

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Dr. D. G. Melrose: Cooling of the Whole Organism.

EDINBURGH CLINICAL CLUB.—At 7, Drumsheugh Gardens, 8 p.m., Professor G. H. Percival: Bullous Eruptions.

GLASGOW UNIVERSITY MEDICO-CHIRURGICAL SOCIETY.—At Glasgow University Union, 7.30 p.m., Honorary Presidential Address by Mr. Roland Barnes.

LIVERPOOL MEDICAL INSTITUTION.—At Liverpool Royal Southern Hospital, 3 p.m., afternoon clinical demonstration.

LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION.—At the Emergency Bed Service, Fielden House, 28, London Bridge Street, S.E., 5.30 p.m., meeting.

OSLER CLUB OF LONDON.—At 11, Chandos Street, W., 7.45 p.m., Colonel L. W. Harrison: Neisser and Neisserian Principles in Venereology; Dr. David Nabarro: The Decline and Fall of Congenital Syphilis. (Meeting in honour of Albert Neisser, January 22, 1855-1916.)

ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Mr. C. Naunton Morgan: Advances in Surgery in Diseases of the Colon and Rectum.

ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Goulstonian Lecture by Dr. G. M. Bull: The Uraemias.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Ophthalmology Lecture by Professor Arnold Sorsby: Outstanding Problems in the Treatment of Ocular Infections.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—At 26, Portland Place, London, W., 7.30 p.m., Professor R. M. Gordon: Symposium on Loaiasis. Speakers will include Mr. W. Crewe, Mr. H. Oldroyd, Dr. B. O. L. Duke, Professor J. J. C. Buckley, Sir Philip Manson-Bahr, Dr. F. Hawking, and Dr. W. E. Kershaw.

ST. ANDREWS UNIVERSITY.—At Physiology Department, Medical School, Small's Wynd, Dundee, 5 p.m., Professor R. E. Tunbridge: Some Problems of Diabetes Mellitus.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., psychiatry demonstration by Dr. Desmond Curran.

WEST LONDON MEDICO-CHIRURGICAL SOCIETY.—At Clarendon Restaurant, Hammersmith Broadway, 8.30 p.m., debate on the Motion: This House considers that Money spent on Research into Rheumatism has been wasted. Proposed and seconded by Dr. Dudley Hart and Dr. C. J. M. Clark; opposed and seconded by Dr. Oswald Savage and Dr. J. Glyn. Preceded by dinner at 7.15 for 7.30 p.m.

Friday, January 21

BRITISH INSTITUTE OF RADIOLOGY.—5 p.m., meeting of medical members.

FACULTY OF RADIOLOGISTS.—At Royal College of Surgeons of England, 5 p.m., Radiotherapy Section meeting. Discussion: Cancer of the Larynx. Openers, Mr. G. S. Seed and Dr. J. R. Nuttall.

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. G. B Mitchell-Heggs: Chronic Granulomas.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., at Institute Lecture Theatre, open clinical demonstration by Mr. Vernon Thompson: Bronchiectasis.

●ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW.—5 p.m., Mr. W. S. Mack: Modern Trends in the Surgery of the Bladder and Prostate.

ROYAL MEDICAL SOCIETY, Edinburgh.—8 p.m., Professor D. M. Dunlop: Present Status of Cortisone in Practical Therapy.

SOCIETY FOR CULTURAL RELATIONS WITH THE U.S.S.R.: MEDICAL SECTION, 14, Kensington Square, London, W.—8 p.m., Dr. Alex. Comfort: Soviet Science; 9 p.m., annual general meeting of section.

Saturday, January 22

BRITISH ASSOCIATION OF ALLERGISTS.—At Royal Society of Medicine, 11 a.m., general meeting. Papers by Professor R. J. S. McDowall, Dr. J. R. Riley, Mr. W. E. Brocklehurst, Dr. F. J. Prime, and Dr. H. G. J. Herxheimer.

APPOINTMENTS

ALDERS, NICHOLAS, M.D., F.R.C.S.Ed., M.R.C.O.G., F.I.C.S., Part-time Consultant Obstetrician and Gynaecologist to Bournemouth and East Dorset Group of Hospitals, South-west Metropolitan Regional Hospital Board (appointment dated June 3, 1954).

COPE, D. H. P., M.B., B.S., F.F.A. R.C.S., Consultant Anaesthetist, the Middlesex Hospital, London, W.

FLEMING, G. M., M.D., D.P.H., Medical Officer, Ministry of Education.

GEDDES, J. E., M.D., Senior Consultant Chest Physician and Supervising Tuberculosis Physician; City of Glasgow Area Western Regional Hospital Board.

HOLMAN, REGINALD ALBERT, M.D., Primary F.R.C.S., Senior Lecturer in Bacteriology, Welsh National School of Medicine, Cardiff.

MCGRATH, S. DESMOND, M.R.C.P.I., D.P.M., Resident Medical Director of St. John of God Private Psychiatric Hospital, Stillorgan, Co. Dublin.

MURPHY, JOHN T., M.B., B.Ch., D.P.H., Medical Officer of Health, Borough of Faversham; Urban District Council of Sittingbourne and Milton; Rural District Council of Swale; Isle of Sheppey Joint (Medical Officer of Health) Committee; Faversham Port Health Authority.

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—J. V. Mainprise, M.B., Ch.B., part-time Assistant Venereologist at Torbay Hospital, Torquay; G. O. M. Neatby, M.R.C.S., L.R.C.P., D.O.M.S., Clinical Assistant in Ophthalmology (S.H.M.O.) at Bath Eye Infirmary; H. I. Leigh, M.B., Ch.B., Registrar in the Department of Neurological Surgery, Frenchay Hospital, Bristol; B. V. Earle, M.D., M.R.C.P., D.P.M., Consultant Psychiatrist in Exeter Clinical Area; H. D. Moore, M.B., B.S., F.R.C.S., F.R.C.S.Ed., Consultant Surgeon in Exeter Clinical Area; I. W. Payne, M.B., Ch.B., F.R.C.S., D.O.M.S., Consultant Ophthalmologist in Plymouth Clinical Area.

WARREN, JOAN E., M.B., Ch.B., Medical Registrar, Worthing Hospital.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Wolff.—On December 15, 1954, at the Whittington Hospital, London, N., to Catherine, wife of Dr. Frederick Wolff, a son—Peter.

DEATHS

Atkinson.—On January 7, 1955, George James Smith Mounay Atkinson, O.B.E., M.R.C.S., L.R.C.P., aged 78.

Brown.—On January 1, 1955, Charlotte Rhoda Hodgins Brown, M.D., of 60, Brockswood Lane, Welwyn Garden City, Herts.

Grieve.—On December 30, 1954, at 53, Beverley Road, Hull, Yorks, Robert Grieve, M.D., F.R.C.S.Ed.

Hardman.—On December 24, 1954, Richard Smith Hardman, M.B., Ch.B., J.P., of "Hopetoun," Chester Road, Woodford, Bramhall, Cheshire, aged 83.

Joekes.—On January 2, 1955, at 16, Stoeplaan, Wassenaer, Holland, Theodorus Joekes, M.B., aged 72.

Lee.—On January 6, 1955, at 39, Ivenhoe Road, Liverpool, Mary Buchanan Lee, L.R.C.P.&S.Ed., L.R.F.P.S.

McCreadie.—On January 3, 1955, at 22, Bankfield Road, Shipley, Yorks, Anthony John McCreadie, *M.C.*, M.B., F.R.C.S.Ed., aged 65.

Macintosh.—On December 28, 1954, at The Gables, Syston, Leicester, Alexander McCheyne Macintosh, M.B., Ch.B., aged 60.

McIntosh.—On December 27, 1954, at 57, Magdalen Yard Road, Dundee, David Glass McIntosh, M.B., Ch.B., M.R.C.P.Ed., D.P.H.

Maclean.—On December 25, 1954, at Newcastle-upon-Tyne, Murdo Maclean, M.B., Ch.B., aged 75.

Moberley.—On December 17, 1954, George Keble Moberley, L.R.C.P.&S.Ed., L.R.F.P.S., of Kloof, Natal, South Africa, aged 83.

Roberts.—On January 8, 1955, the result of an accident, Adeline Mary Roberts, O.B.E., M.D., J.P., late of Welbeck Hotel, London, W.

Rundle.—On December 24, 1954, at his home, Green Borders, Looe, Cornwall, Claude Rundle, O.B.E., M.D., D.P.H.

Somerset.—On December 27, 1954, William Ralph Somerset, M.B., Ch.B., of Wolverhampton, Staffs, aged 80.

Stewart.—On January 2, 1955, at Dial House, Bourton-on-the-Water, Glos, Robert Bell Stewart, *M.C.*, M.B., Ch.B., D.P.H., D.T.M.

Sweet.—On December 27, 1954, Samuel Henry Sweet, M.R.C.S., L.R.C.P., of Heston Lodge, Heston, Middlesex.

Webber.—On December 24, 1954, at University College Hospital, London, W.C., Harald Norris Webber, B.Chir., F.F.A. R.C.S.

Any Questions ?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Treatment of Salmonella Carriers

Q.—*We have lately had an epidemic of enteritis in this area, and Salmonella typhi-murium has caused a number of cases apparently. The patients are now all symptomless and very fit, but the public health authorities are excluding children with the salmonella in their stools from school for weeks and sometimes months. I am urged to treat the children with succinylsulphathiazole, then sulphadiazine, then chloramphenicol, and finally oral streptomycin if the carrier state has not meanwhile settled. This regime does not seem effective in many cases. Can you advise me, please?*

A.—The treatment of the salmonella carrier state has always been a troublesome problem, and no infallible solution to it is known. In attempts to eliminate an organism altogether, as distinct from suppressing its growth during an acute infection, an actively bactericidal drug is preferable to one which is only bacteriostatic, and on this ground oral streptomycin is the most promising of the three treatments mentioned. It might well be tried first instead of being used as a last resort. The dose should be 0.5 or 1 g. according to age, four times a day for five days. Recently American workers have recommended combinations of oral antibiotics for treating intestinal conditions, and a mixture of streptomycin or neomycin and polymyxin (e.g., streptomycin 250 mg., polymyxin 200,000 units, in each dose) might well be tried, although, so far as we are aware, this would be purely experimental. All these antibiotics are unabsorbed when given orally, and there is thus no risk of toxic effects. They act only in the bowel, and would therefore be ineffective if the infection involved the biliary passages, as it sometimes does. Although antibiotics, when given parenterally, are excreted in the bile, some in high concentration, there is probably no drug treatment which can be depended on to cure the carrier state when it involves this area.

Surgery in Congenital Pulmonary Stenosis

Q.—*What results may be anticipated from the surgical treatment of congenital pulmonary stenosis? What cases are suitable for surgery, and at what age should operation be performed? What regime is advised for infants and children awaiting operation?*

A.—It is impossible to answer all the problems contained in this question in a short paragraph. The term "pulmonary stenosis" is a generic one covering various types of abnormality. There are considerable differences in both the clinical features and the management of those due to a pulmonary valve stenosis with a normal aortic root and those of the Fallot group in which the stenosis is associated with a ventricular septal defect.

In general, operation should be considered in all cases of pulmonary stenosis unless the condition is very mild or unless the patient is *in extremis* or has other grave defects. Cases of pure pulmonary valve stenosis should be operated on, however young the patient, if the condition is severe enough to satisfy general criteria. In the Fallot group it is generally better to wait until the age of 4 or 5 years, unless there are grave features, such as severe cyanosis or syncopal attacks.

While waiting for operation the children need chiefly the general care and protection from physical strain that most parents are only too eager to accord; special medical attention includes avoidance of the perils of catarrhal and other infections; these children are especially prone to upper and lower respiratory infection. In spite of the polycythaemia iron may be needed.

Surgery offers hope of great relief, where before there was none. In good hands the mortality is not high, ranging from 5–15% for mild to severe cases. The results are good or excellent in about 70% of survivors; the child may appear completely normal in every way. Certainly life is transformed for both the child and the parents. When the cardiac lesion is complicated (for example, tetralogy of Fallot) the late prognosis is as yet uncertain. Operations have not yet been done for as long as ten years, and a longer time must elapse before this can be assessed. In cases of isolated pulmonary valve stenosis treated successfully by valvotomy the late prognosis is probably excellent.

Toxic Effects of Amphetamine

Q.—*What toxic effects may arise from prolonged use of dexamphetamine sulphate? I am particularly interested to know whether there is any risk of blood or hepatic changes, chronic dyspepsia, carcinogenesis, and such-like serious effects.*

A.—The actions and toxic effects of dexamphetamine sulphate are similar to those of amphetamine sulphate, but the D-isomer is claimed to be effective in smaller dosage. Both substances have been safely used for lengthy periods in narcolepsy or obesity in doses up to 60 mg. daily. The development of psychoses has been reported, as for example in the man of 49 who had taken 250 mg. daily for five years. Reports have also appeared of damage to bone marrow: panhaemocytopenia occurred in a girl of 21, and acute aplastic anaemia in a man of 26 who took 290 mg. during 19 days. Habituation may also occur, though this is probably not very common. Withdrawal symptoms observed included hallucinations, restlessness, and insomnia. These symptoms, together with anorexia, may be expected to follow prolonged administration in most patients. Many of those receiving amphetamine possess personality defects and may be especially prone to exhibit these side-effects. Tachycardia and hypertension have also been reported, but I am not aware of any evidence of carcinogenesis or liver damage from prolonged use of dexamphetamine.

*** This answer is taken from the third book of *Any Questions?* Copies of both the second and third books of *Any Questions?*, each containing some 200 expert answers, are available from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or through any bookseller, price 7s. 6d. a copy (postage 6d.). The third book contains a cumulative index.

Blushing

Q.—*A girl of 19 who appears to be perfectly healthy has complained for the last year of involuntary blushing. This occurs regularly every afternoon and sometimes during the evening. There is a feeling of burning of the skin of her face and neck, which become suffused with blood and remain so for an hour or so. There seems to be no association with digestion: the blushing happens after a very light lunch or even no lunch at all. Nor is there any menstrual disturbance. She has a fair, healthy skin, is active and intelligent, and has no sign of thyroid dysfunction. Her main complaint is of getting her leg pulled unmercifully.*

A.—Not much is known of the physiological mechanism of blushing, except that it is not affected by cervical sympathectomy. It is probable, however, that the mechanism of capillary dilatation over the blush area is inherently less stable in some people than others. In view of the fact that the girl is healthy, one can presumably exclude gross lesions such as hypertension, polycythaemia, phaeochromocytoma,

carcinoid tumour, and the like. The condition must therefore be an exaggeration of the normal act of blushing, which, the psychiatrists tell us, is incompatible with complete innocence or modesty. It is supposed to occur typically in individuals in whom there is conflict between morality and sexual impulses and to be particularly common and severe at phases of life when these conflicts are especially acute. It is often associated with feelings of inferiority, and teasing is therefore quite the worst treatment. "Shyness springs from secret shame," and it would be worth trying to discover tactfully whether the lady has some such secret. An inquiry into the first onset of the symptom and the reason for its occurrence in the afternoon and evening might be helpful.

Prosthesis after Mastectomy

Q.—*What is the best method to adopt after mastectomy to provide a natural and comfortable bust? Most supports lift upwards on the operation side owing to the lack of weight and in spite of artificial padding.*

A.—I do not think there is any real difficulty in fitting artificial breasts. Many firms supply good ones, matching exactly the breast on the other side. They are made of sorbo rubber and are contained in washable covers. Any tendency to lift can be prevented by hooking the lower edge of the cover to the corset or other garment. No method of plastic remodelling of the removed breast is altogether satisfactory, and reliance should always be placed on some such prosthesis.

Two Cases of Fetishism

Q.—(*a*) *A wife has asked my advice about her husband, aged 40 years. They have been happily married for 16 years, have three children, and have enjoyed a completely satisfactory sexual life. However, the husband, an apparently healthy, athletic type, has always shown a strong desire for his wife to wear, on occasions, only various plastic and rubber raincoats, etc. She has been quite happy to acquiesce to his wishes until she read somewhere that it indicated some type of mental disease and must therefore stop, in case it "leads to something worse." She is rather frightened to let her husband know that she has mentioned her husband's peculiarity, and really only wants reassurance. Is there any book which might help to give some semblance of a sensible answer to these and other similar problems should they crop up?* (*b*) *A boy aged 5 years has since infancy shown an abnormal desire to touch and handle silk. His mother had hoped this little habit would have disappeared as he grew up, but the reverse is the case. Very embarrassing situations are arising, as he is not averse to touching clothing of complete strangers. Already there has been some trouble at school, as he has gone so far as to "borrow" little girls' ribbons and has taken home quite a collection of them. He has also been touching the clothing of women in shops and buses. Should I advise psychiatric advice or let well alone? The mother is quite willing to "do anything."*

A.—(*a*) The wife in the first question may be reassured. Her husband's peculiarity is a form of sexual disturbance termed *fetishism* in which the sexual feelings are aroused in association with an inanimate object. This well-known condition, which appears not to occur in women, dates from early childhood and may be associated with emotions concerning breast feeding or with fantasies concerning the female genital organs. The condition is often relieved by psychotherapy. It is not a mental disease but a symptom of emotional disturbance. Nor is the symptom the forerunner of "something worse," which presumably means the type of sexual perversion reported in the sensational press. Rubber and plastic raincoats, often of black material, women's shoes, and corsets and many other articles of women's attire are common fetishistic objects. The husband should be advised to consult a psychiatrist if he finds his condition distressing. But this may be impracticable. Meanwhile the couple may resume marital relations, under the old conditions, in the certainty that no disaster will befall them.

(*b*) The second question concerns a fetishism for silk. The "little habit" is not likely to disappear spontaneously. The mother should at once get advice at a child guidance clinic. As he grows older the boy will learn to control the wish to touch and handle silk. But he may collect silk ribbons, etc., and keep them secretly and obtain erotic pleasure by feeling them. The habit and urge, although personally distressing and even hated, can acquire a compulsive power difficult to resist. The husband mentioned in the former question can probably recall childhood experiences comparable to those of the little boy of 5.

Fetishism and allied topics are described in *Mental Health and the Psychoneuroses*, by Dr. J. A. Hadfield (Allen and Unwin, 1953), and in *The Sexual Perversions and Abnormalities*, by Dr. Clifford Allen (Oxford Medical Publications, 1949).

Treatment of Meningococcal Meningitis

Q.—*What is the accepted treatment of meningococcal meningitis? Has intravenous oxytetracycline ("terramycin") any place in its treatment?*

A.—Sulphonamides are usually sufficient. For a severe infection in an adult give 2 g. "soluthiazole" (a soluble form of sulphathiazole) intravenously along with 1.5 g. sulphathiazole by mouth: repeat the oral dosage every four hours for three days, reducing to 1 g. six-hourly for a second three days. Alkaline fluids should be given by mouth throughout the course. Penicillin is not usually required, but if the cerebrospinal fluid is turbid it is sound practice in any meningeal illness to give 10,000 to 20,000 units intrathecally at the first lumbar puncture pending laboratory reports on the causal organism: if meningococci are reported, further penicillin is rarely necessary. Chloramphenicol given by mouth readily passes into the cerebrospinal fluid and has been used successfully in the treatment of meningococcal meningitis, but, on the score of expense and toxicity, has no advantage over sulphonamides. There is no obvious place for intravenous oxytetracycline. In *Prescribers' Notes* issued by the Ministry of Health for November, 1954, meningococcal meningitis is listed (p. 85) as one of the infections in which chlortetracycline ("aureomycin") and oxytetracycline ("terramycin") are *not indicated*, being less suitable than sulphonamides.

Tincture of Belladonna

Q.—*I have a patient who is taking 5 minims (0.3 ml.) of tincture of belladonna each day as an antispasmodic. Is it possible that this dose could be cumulative in its effect?*

A.—This dose of tincture of belladonna is equivalent to 1/600 gr. (0.1 mg.) of atropine. It would be wholly destroyed and excreted in 24 hours and would not be cumulative.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs. Authors overseas should indicate on MSS. if reprints are required, as proofs are not sent abroad.

ADVERTISEMENTS should be addressed to the Advertisement Manager, B.M.A. House, Tavistock Square, London, W.C.1 (hours 9 a.m. to 5 p.m.). TELEPHONE: EUSTON 4499. TELEGRAMS: *Britmedads, Westcent, London.*

MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the Association. TELEPHONE: EUSTON 4499. TELEGRAMS: *Medisecra, Westcent, London.*

B.M.A. SCOTTISH OFFICE: 7, Drumsheugh Gardens, Edinburgh.